

ANNALS OF SURGERY

VOL. 112

SEPTEMBER, 1940

No. 3



CONGENITAL ANOMALIES OF THE DUODENUM

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CONGENITAL ANOMALIES of the duodenum are of sufficient rarity and interest to warrant a report when encountered. We have had the fortune to

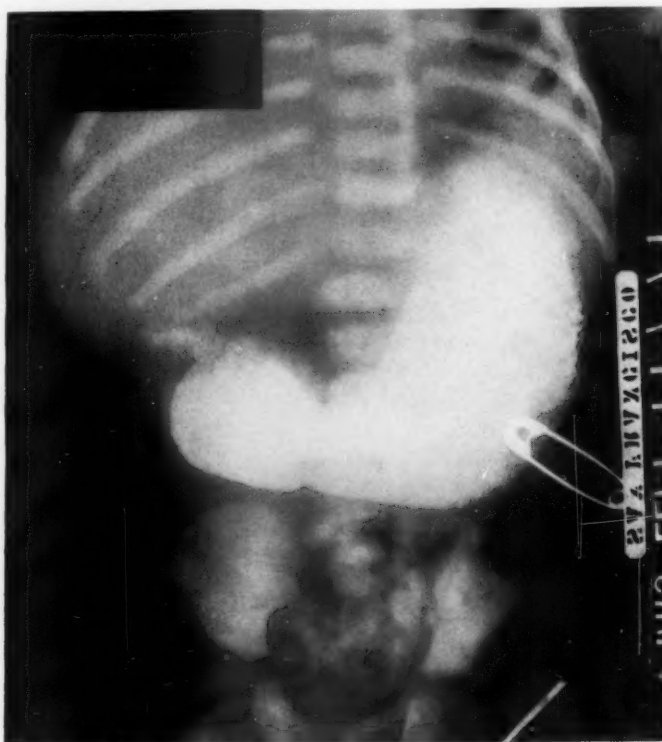


FIG. 1.—Case 1: Radiograph three hours after barium meal showing almost complete retention. A minute quantity of barium has passed into the proximal jejunum.

examine and study, in some detail, three cases. These cases have offered the opportunity of assessing the various theories as to their etiology and of

Submitted for publication June 29, 1939.

examining, in this respect, several details of duodenal development which serve to clarify the subject. In addition, a short review of the classification, incidence, diagnosis and treatment of such anomalies is considered.

The following is a short résumé of the three cases which prompted our interest in this subject. The first of them illustrates an example of congenital

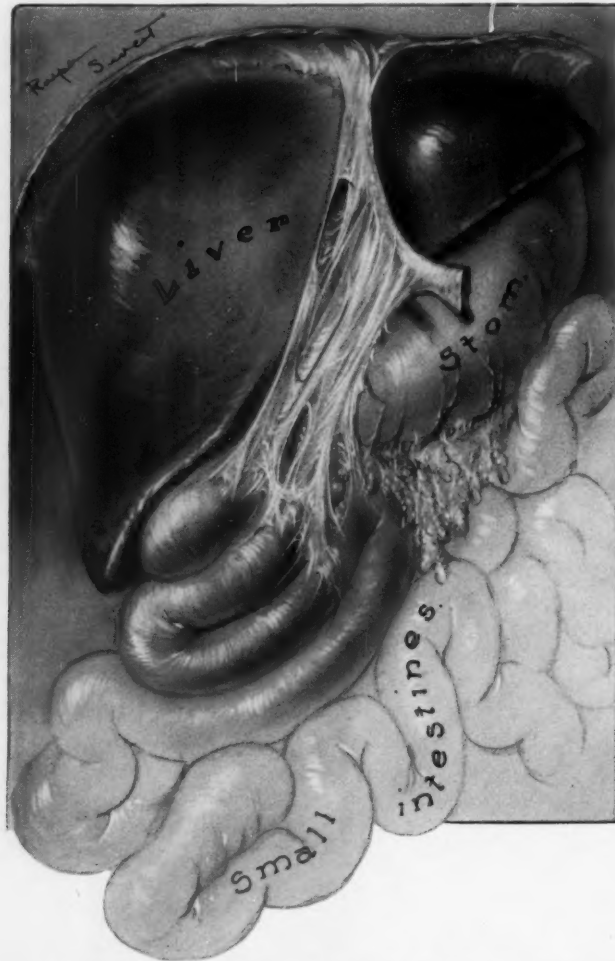


FIG. 2.—Appearances on opening abdomen in Case 1. The hepato-duodenal adhesions fix the coiled duodenum against the greater curvature of the stomach. The colon is not visible as owing to nonrotation it lies behind and to the left of the small bowel.

duodenal stenosis associated with nonrotation of the intestine; the second, of congenital duodenal valve formation, and the third, a case exhibiting abnormalities of shape, position and fixation. All these cases were associated, as is so common in congenital malformation, with other anomalies.

Case 1.—Baby H., male, birth weight 7 lbs. 10 oz. The baby was spontaneously delivered at term, markedly jaundiced. Meconium was passed at the end of the first 24

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hours. On routine formula, the infant nursed poorly. On the third day, the child regurgitated large quantities of sour-smelling food but passed a large brownish-yellow stool. From the third to the seventh day, he vomited repeatedly. The intensity of the jaundice increased and the child rapidly lost ground. There was a weight loss of 18 oz. by the seventh day.

Physical Examination.—March 26, 1938: There was considerable loss of tissue turgor and deep icterus. The abdomen was distended in both upper quadrants and reversed gastric peristalsis was observed after feeding. No pyloric tumor was palpable but considerable gastric dilatation was determined. There was bilateral talipes equinovarus. Radiographic examination revealed dilatation of both esophagus and stomach with con-

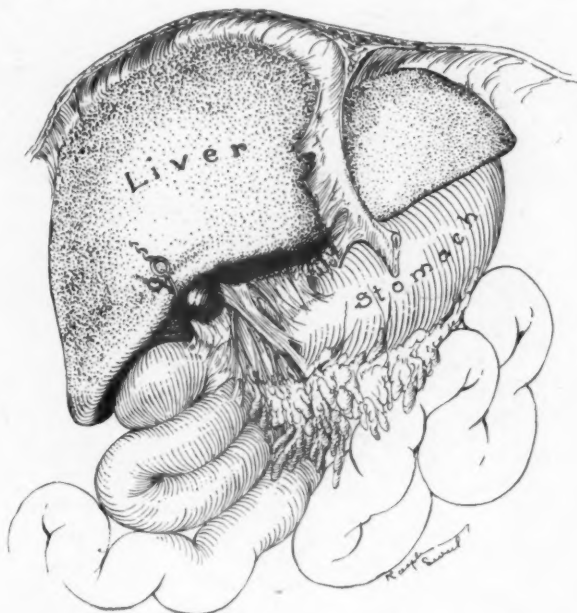


FIG. 3.—Case 1: Following division of peritoneal adhesions.

siderable food retention. No barium passed the pylorus. At three hours, retention was almost complete (Fig. 1.). However, a minute quantity of barium was seen in the proximal jejunum. *Preoperative Diagnosis:* Pyloric stenosis or spasm.

Operation.—March 26, 1938: Following preoperative supportive measures celiotomy was carried out. The liver presented early and although of normal size, its unusually mottled brownish color was noted. The transverse colon was absent from its usual position below the greater curvature of the stomach, being replaced by coils of small intestine. The colon was found accumulated on the left side, indicating nonrotation. The pyloric region was obscured by a persistent hepatoduodenal ligament (Fig. 2). On division of this peritoneal ligament, the duodenum was found matted together by adhesions in the form of an S-shaped loop and fused with the greater curvature of the stomach below the pylorus (Fig. 3). On further dissection the curvature of the duodenum was restored, it being found to be unfixed, suspended by a mesoduodenum.

A stenotic area, three-quarters of an inch long, reducing the bowel caliber to one-eighth of an inch, involved the proximal segment of the second and distal portion of the first part of the duodenum (Fig. 4). On longitudinal incision of this area, a lumen the size of a pencil lead was encountered. The openings of the pancreatic and biliary ducts were not observed. The diameter of the lumen was increased by closure of the incision

transversely, as in the Heinecke-Mikulicz procedure, and the lumen now judged to be of adequate size. After closure the child was returned to bed in fairly good condition.

The postoperative course was uneventful, except that the infant vomited once on the second day. He was discharged on the seventh postoperative day.

Subsequent Course.—Fifteen days after operation the child died, following a convulsion associated with a respiratory infection. Autopsy was refused. Jaundice, though decreasing, persisted up to the time of death.

Case 2.—S. M. W., age 7½, white, was brought to the University of California Hospital, because of frequent and persistent vomiting since one month following birth. The

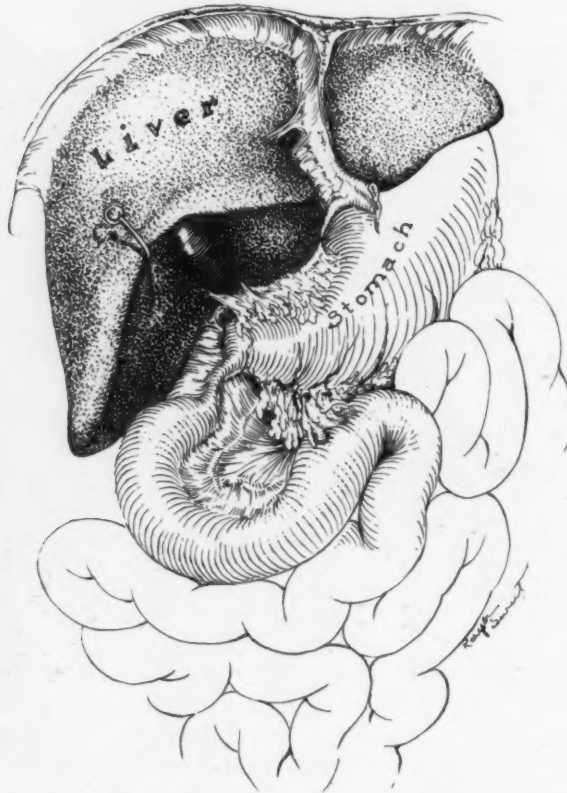


FIG. 4.—Case 1: The duodenal loop has been freed by further dissection of adhesions. The stenotic area and the unfixed mesoduodenum are clearly shown.

child had been apparently normal up to the age of one month, at which time she began to have spells of projectile vomiting following each feeding. During the next two months the child dropped from a birth weight of 7¾ lbs. to about 4 lbs. At the age of three months, the child was taken to a private hospital where she remained for the next nine months. The vomiting continued and her weight increased to 9 lbs. At 15 months, vomiting persisting, a preoperative diagnosis of congenital hypertrophic pyloric stenosis was made and celiotomy performed. Examination revealed a large gaping pylorus, many veil-like adhesions from the gallbladder to the duodenum, a large mesoduodenum and a uniform collapse of the distal two-thirds of the duodenum and small intestine. Many enlarged lymph nodes, thought to be tuberculous, were found in the mesentery. A long Meckel's diverticulum was present. There was no operative intervention and a postoperative diagnosis of "tuberculosis of the mesentery and intestines" was made.

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Subsequent Course.—The child remained a hospital case until the age of three, continuing to vomit, and on discharge her weight was only 18 lbs. For the following four years, up to the age of seven, and her entry into the University of California Hospital, the child continued to vomit after each meal, at times bringing up food eaten several days previously. She gained weight slowly, and was constantly under medical care for seven years. Physical examination on entry showed an underweight, pallid, dehydrated child. No visible peristalsis or palpable organs. No other positive findings. Laboratory data were essentially normal, including a negative tuberculin test. Radiographic examination, made on entry, seemed to indicate a definite obstruction in the second or third portion of

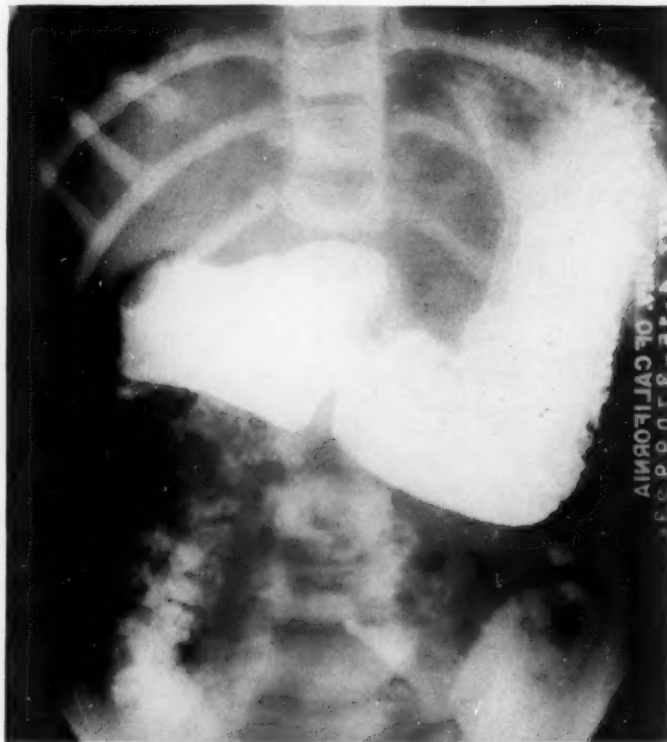


FIG. 5.—Case 2: Radiograph three hours after barium meal showing dilated stomach and megaduodenum with obstruction.

duodenum. (Fig. 5.) *Preoperative Diagnosis:* Congenital stenosis of the second or third part of the duodenum.

Operation.—April 19, 1937: The transverse colon and omentum appeared to be normal. The mesentery of the small bowel and duodenum contained many hard, enlarged lymph nodes of varying size. The entire small bowel distal to the ligament of Treitz was moderately collapsed and appeared quite normal. The stomach was markedly dilated and flabby and extended well down into the pelvis. The stomach walls were very thick. The pylorus admitted three fingers, and the first and a part of the second portion of the duodenum were markedly dilated and hypertrophied. The common bile duct was moderately dilated and entered the duodenum at an abnormally high position. The cecum had not descended from under the liver and was suspended by a mesentery.

In view of the foregoing findings it was decided that the procedure of choice was mobilization of the duodenum to determine the cause and site of the obstruction rather than a palliative gastro-enterostomy. Upon freeing and rolling up the duodenum, a

circular ring of constriction, four inches distal to the pylorus, was found. The third and fourth portions of the duodenum distal to this constriction were of normal size. An incision was made directly over the constricted area and a diaphragm was encountered, completely occluding the lumen save for a small perforation anteriorly, which barely admitted the tip of the little finger. The diaphragm was completely excised and the bowel was closed in the Heinecke-Mikulicz manner to prevent stenosis. The child did extremely well postoperatively; taking food by mouth without vomiting and rapidly gained in weight. When last seen, March 29, 1939, two years later, she had no gastro-intestinal symptoms and was now up to normal weight for her age.



FIG. 6.—Appearances in Case 3 viewed from below and the right. The cecum is fixed to the under surface of the liver and below it the highly constricted and obstructed duodenum may be seen.

Case 3.—A. C., female, age 3 weeks, was brought to the University of California Hospital, August 6, 1934, because of a large, protruding umbilical mass and persistent projectile vomiting for the two weeks previous to entry. The child was born at term and delivered normally. The umbilical mass was observed at birth. It slowly increased in size and became gangrenous. Foods were poorly taken, the child exhibiting projectile vomiting at the end of the first week, which continued until the time of hospital entry. At entry, the child was markedly emaciated and dehydrated. The umbilical mass was large, dark brown, cylindric in shape, protruding some three inches beyond the abdominal wall. It was covered by a thick, hard seal, from beneath which a foul-smelling, brownish, serous fluid exuded. The mass was kept under considerable tension by intra-abdominal pressure. There was a ring of unhealthy granulation tissue at the junction of the mass with the abdominal wall. Methylene blue given orally did not appear in the mass or its

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discharge. After routine preoperative care, the protruding gangrenous tissue was removed; the area left gradually granulating in, and the child was discharged, September 16, 1934. Pathologic examination of the material showed the presence of liver tissue.

Subsequent Course.—During the next three months, while at home, the child did poorly, vomiting at frequent intervals. On December 15, 1934 she was returned to hospital. The umbilical wound was well healed although marked divarication of the rectus abdominus muscle was noted. Vomiting continued and on January 9, 1934 the child contracted a bronchopneumonia from which she expired, January 11, 1935.

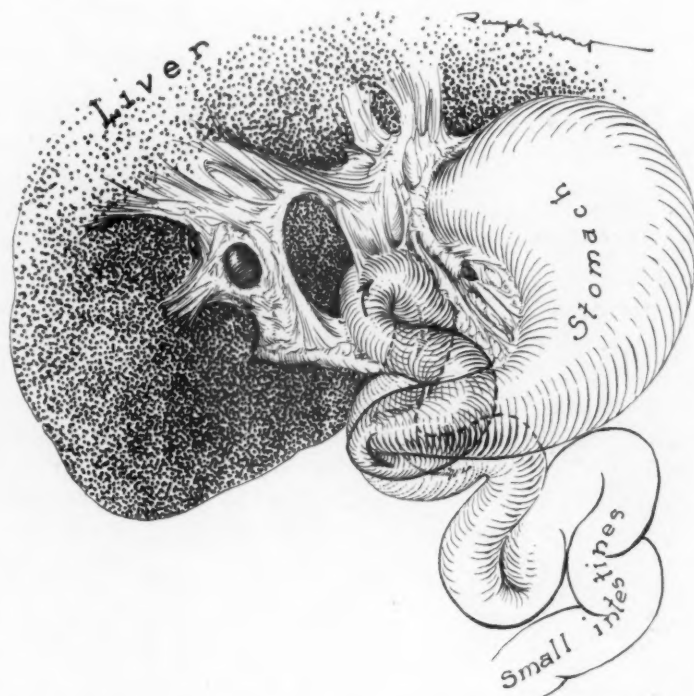


FIG. 7.—Case 3: Semidiagrammatic illustration showing the position and convolution of the abnormal duodenum.

Autopsy (Fig. 6).—The liver was extremely large and hard, and extended down to the upper limits of the right iliac fossa. There was a scarred area on the anterior surface of the liver in the region of the umbilicus, obviously the area of herniation. There was an anomalous right lobe of the liver. A single umbilical artery extended from the hypogastric vessels to the liver where it entered an abnormal porta hepatis. The artery was elevated from the posterior surface of the anterior abdominal wall, being enclosed in a mesentery. It formed, with the posterior abdominal wall, a boundary which divided the peritoneal cavity into two parts, a small right and a large left portion. The alimentary tract exhibited incomplete fixation. The stomach was of normal size and occupied its approximate normal position. There was a marked duodenal anomaly present. The first portion extended horizontally to the right and was then abruptly reflected upon itself, in the form of a U, to the region behind the pyloric antrum. It then ascended obliquely upward and to the right, making an abrupt flexure behind the liver to extend in a sharp curve, downwards and to the right, making still another flexure behind the first portion of the duodenum, and passed horizontally to the left where it terminated in the duodenojejunal flexure (Fig. 7). It was interesting to note that in this case the

duodenum was so markedly convoluted as to mechanically offer obstruction despite the complete lack of actual peritoneal fixation.

Congenital obstruction of the duodenum received much attention in the latter half of the last and at the beginning of the present century. This was to be expected as the outcome of the reconstructive methods introduced into embryology by His, in 1868. Comprehensive articles were published on the continent by Theremin⁴¹ (1877), Kuliga²⁹ (1903) and Kreuter^{27, 28} (1905, 1909); in America by Cordes⁸ (1901); and in England by Clogg⁷ (1904) and Spriggs³⁸ (1912). The foremost recent discussions are those of Davis and Poynter⁹ (1922) and of Ladd³⁰ (1933).

It is difficult to determine with any accuracy the number of cases reported as the literature is in some confusion. Spriggs,³⁸ however, stated, in 1912, that congenital duodenal obstruction "is not so very much rarer than imperforate anus as one might expect, the one affection being so obvious cannot be missed, the other most certainly is not so constantly in the mind of the practitioner and not so obvious, hence it often is missed." That the duodenum is a common level of congenital obstruction is indicated by Davis and Poynter.⁹ These authors studied 392 cases of congenital intestinal obstruction, of which 134 occurred in the duodenum.

Attempts have been made to estimate the incidence of congenital obstruction in the general population at infancy. Again the figures are too unreliable to be of much service except to indicate the comparative rarity. Such figures are given by Ernst¹¹ (1916), two cases of intestinal atresia in 41,000 children in the Royal Lying-In Hospital, Copenhagen; and Theremin,⁴¹ nine cases in 150,000 at Petrograd, and two in 111,451 born over an 11-year period at Vienna.

Pathology.—Pathologically congenital duodenal obstruction has been found to result from the effects of either intrinsic or extrinsic factors.

Extrinsic obstruction of the duodenal lumen has been described as the result of either developmental error or prenatal pathologic processes. Among developmental errors may be listed kinking of the bowel from lack of fixation or abnormal fixation, massive volvulus, persistence of a hepatoduodenocolic ligament, annular pancreas and vascular anomalies with aberrant vessels. Among prenatal pathologic processes which have been encountered may be mentioned abnormal adhesive bands, mesenteric cysts and neoplasms of related organs such as the liver or pancreas.

Intrinsic obstruction is the outcome of atresia, amounting in some instances to complete suppression of a segment of the intestine, stenosis, or valve formation. It has been stated (Cordes⁸ and Clogg⁷) that complete atresia is more frequent than stenosis in all situations, and that both atresia and stenosis are much more frequent than valve formation. These forms are sometimes associated with abnormalities of the biliary tract. The bile duct may have an abnormal site of implantation, draining on occasion into the stomach or entering the duodenum at an unusually low level. In some instances doubling of the bile duct has been reported, each duct emptying at a different level. In-

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trinsic obstruction occurs either above, at, or below the ampulla of Vater. It is impossible to give any very satisfactory opinion of its frequency at any level. It would seem, however, that the great majority of obstructions occur in the second portion of the duodenum immediately above or immediately below the duodenal papilla. Davis and Poynter⁹ cited 59 cases above and 75 below; Cordes,⁸ 20 above and 13 below. The exact location is so frequently not reported that statistical conclusions are impossible. A small percentage of cases of duodenal atresia or stenosis are associated with stenosis or atresia of one or more segments of the alimentary tract.

In extrinsic obstruction the etiologic factor is so readily demonstrable, either at the operating or postmortem table, as to require no further comment.

For intrinsic obstructions, however, a wide variety of theories, many now of only historic interest, have been propounded. Such views include fetal intussusception, enteritis, localized spasm, Meckel's discarded segmentation theory, segmental atrophy, local vascular thrombosis or embolism, hypertrophy of the valvulae conniventes, *etc.*

A theory widely held is based on the dictum of Bland-Sutton³⁹ that abnormalities tend to occur at the sites of embryologic events. As the biliary and pancreatic systems arise from the second part of the duodenum, this view has been accepted as the determining factor for the presence of the obstruction at this level or in its immediate neighborhood. This theory has the attraction of simplicity and is without doubt, for some regions of the body, such as the branchial region, of the greatest significance. In this instance, however, we find the theory highly questionable if not wholly unacceptable, as the greater percentage of intrinsic obstructions of the duodenum occur relatively distant from the entrance of the biliary duct. In addition, exactly similar pathologic processes, occasionally concomitant, occur at other levels of the small intestine where development is unassociated with any special embryologic event in the Bland-Sutton sense. The pathologic processes being the same, it is reasonable to suppose that the factors responsible for atresia or stenosis in the duodenum and at other levels of the bowel are similar.

A hypothesis which requires more serious consideration because of its almost universal acceptance is the outcome of observations made by Tandler,⁴⁰ in 1900, on the formation of the duodenal lumen. This author pointed out that during development the duodenal lumen becomes completely obliterated (fifth to sixth week) by an extraordinary proliferation of its epithelial lining. This proliferation appears to completely block the lumen although this has been questioned by Frazer.¹³ It has been assumed (Kreuter²⁷) that persistence of this state is responsible for atresia, stenosis and membrane formation. However, similar objections arise as in Bland-Sutton's theory, for atresias occur at levels which are stranger to such a process of proliferation.

Wyss has propounded a view that the disturbance is the outcome of interference with vascularization and often associated with changes in the vascular pattern. He describes two cases with absent pancreaticoduodenal arteries. This view is not to be confused with extrinsic obstructions caused by

anomalous vessels. It is well recognized that changes in vascular pattern are common in congenital anomalies but this does not mean that the changes are the primary cause of the anomaly and have not arisen secondary to the deficiency in the area supplied by the vessel.

Embryology.—It goes without saying that a necessary preliminary to an understanding of anomalies of position, and to a discussion of the possible mechanism of atresia or stenosis, is a review of the chief events in the developmental history of the duodenum. The outline of events herein described is based upon a series of dissections of the embryo at various stages, carried out

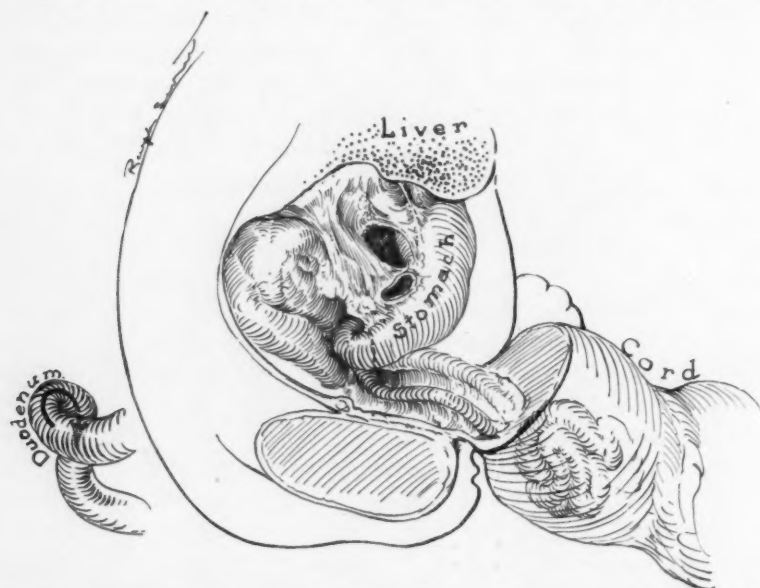


FIG. 8.—Dissection of an embryo of 13.5 Mm. C.R. length viewed from the right anterior aspect. The liver has been excised exposing the opening of the omental bursa and the severed portal vein. Note the formation of the primary duodenal curves at this stage. The enterocolic segment occupies the umbilical cord. Inset shows the simplicity of the primary curves.

under the microscope. It is felt that such a method gives a far more accurate picture of morphologic details than the more usual technic of reconstruction.

We have found it convenient to divide the development of the duodenum into four stages:

Stage I.—Rudimentary Stage: At this stage the duodenum is recognized as the segment of the primitive gut lying between the dilatation of the stomach and the commencement of the enterocolic loop. We regard the duodenal segment as constituting, at an early stage, a distinctive part of the alimentary tract. Supported by a thickened portion of the common dorsal mesentery, the biliary system has already made its appearance, and at 5 Mm. the dorsal pancreatic rudiment has budded into the mesoduodenum.

Stage II.—Formation of Primary Curves (Fig. 8): As development proceeds, the stomach undergoes rotation to assume its permanent position, and as it does so, the future omental bursa is defined. Meanwhile the enterocolic

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loop has elongated and proceeded to occupy its position at the root of the umbilical cord. The duodenum has likewise participated in the changes. These involve predominantly its first portion. This part shows a far greater degree of elongation than the rest. At 13.5 Mm. it is large and well developed and is almost twice the diameter of the succeeding portion of the intestine. It extends transversely across the abdomen with a very slight upward inclination and is highly arched over the vitelline or future portal vein. Passing dorsally, it

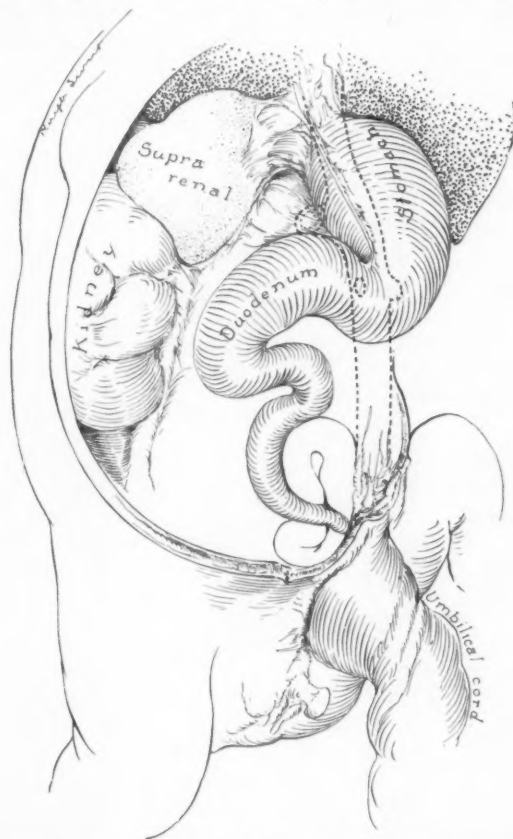


FIG. 9.—Dissection of a 43 Mm. C.R. length embryo viewed from the right anterior aspect. The liver has been removed. The elongation and increase in size of the duodenum is extending into its second portion in the establishment of the secondary duodenal curves. The umbilical vein is indicated in dotted outline. The prearterial segment of the enterocolic loop is about to return into the abdominal cavity.

terminates by making a sudden flexure opposite the wolffian body (mesonephros). This flexure is the future duodenojejunal flexure. The duodenum as a whole is shaped rather like the letter U placed horizontally with its convexity ventrally and with the vitelline vein lying in its concavity. The second portion of the duodenum is extremely short and inclines a fraction to the right to enter the third and fourth portions, which are represented by little more than a slight curve at the future duodenojejunal junction. Under the

influence of the increase in size of the body cavity, the determination of the position of the stomach and the enlargement of the future portal vein, the essentials of the permanent curvature of the first portion of the duodenum have been established.

Stage III.—The Duodenal Loop, (Fig. 9): The stage initiating the establishment of the duodenal loop and the attainment of its adult form is characterized by the very rapid development and elongation of the second portion of the duodenum and slightly later of the two succeeding parts. At this time, various observers (Tandler,⁴⁰ Johnson²⁰) have noted in the lower two-thirds

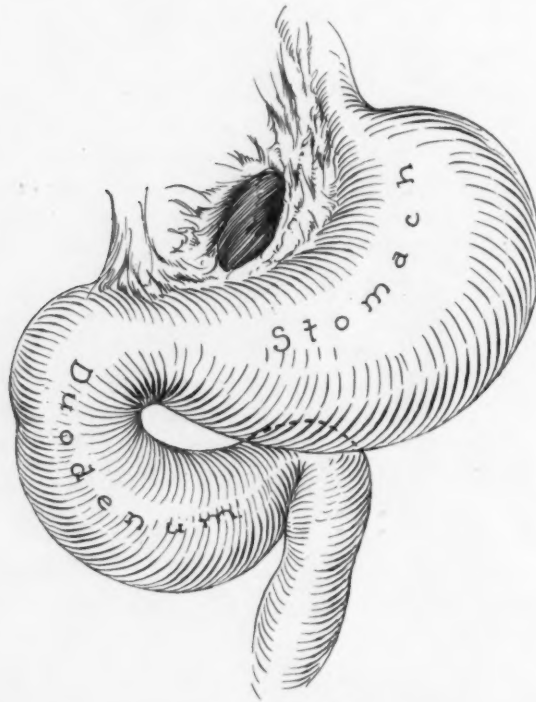


FIG. 10.—Dissection of a 43 Mm. C.R. length embryo. The enlargement and elongation of the duodenum has extended to the third and fourth portions. The duodenal loop still exceeds that of the jejunum in diameter. The duodenojejunal flexure has crossed to the left of the midline.

of the duodenum, overgrowth of the epithelial lining amounting to an actual occlusion of the duodenal lumen. Vacuolization follows, 22–24 Mm., leading to reestablishment of the lumen and formation of the villi. At 30 Mm., the vacuoles having coalesced, the lumen is pervious throughout. Differential growth has resulted in the elongation of the ligament of Treitz and the transference of the duodenojejunal flexure to the left of the midline (Fig. 10). Hunter,¹⁷ in this connection, stresses the importance of the part played by fixation bands in the formation of the duodenal curve. Frazer,¹³ criticizing this view, believes that the curve is produced under the influence of the

growth of the head of the pancreas. We, however, do not subscribe to either of these views and regard the curvature of the duodenal loop as due to differential growth factors and time relationship rather than to mechanical effects.

Stage IV.—Fixation: The final stage concerns the ultimate placement of duodenojejunal flexure and fixation of the gut. The mesoduodenum has closely approximated the dorsal parietal peritoneum by the development of the pancreas between its layers, and fusion ensues. The adhesion is no doubt influenced by the returning gut. The transverse colon during the rotation of the extra-abdominal intestine is carried over the duodenum and adheres to it at the point of crossing.

The Genesis of Duodenal Anomalies.—We have thought it advisable in view of the impossibility in the present state of our knowledge of making any definite statement as to ultimate cause, to relate the various errors in terms of the various stages of duodenal development previously discussed. In addition, certain general principles need emphasis. It should be recognized that such fundamental processes as growth and differentiation proceed independently of one another and may show varying velocities of change. There is ample evidence to show that the original control of differentiation appears to be exerted in relation to definite morphogenetic fields and is dependent, not upon any definite localization, but upon the position of any part relative to the whole structure or on the levels which the various parts occupy along an axis of development. It is perhaps safe to assert, judging from experimental evidence, that there are, for the alimentary tract, critical periods which precede differentiation and which differ in time in different parts of the gut. The ultimate effects produced in the way of errors are influenced by the relationship of the time of action of the noxious agent to the stage of differentiation attained.

Anomalies of the first stage are those associated with the development of the biliary and pancreatic rudiments resulting in such conditions as dichotomy of the bile duct and annular pancreas. In the former it is probable that the same influence that establishes the biliary anomaly is responsible for the associated atresia or stenosis of the duodenum. In the latter deformity any delay in the appearance of the ventral pancreatic rudiment from the duodenum is envisaged as forcing this portion of the pancreas to follow the further development of the duodenum rather than the dorsal rudiment. Both of these anomalies are regarded as having their origin in the earliest stages of development.

Anomalies of the second stage associated with the development of the first part of the duodenum are almost unknown. We have been unable to find records of a single instance of atresia or stenosis affecting this portion. Such freedom from error is not unexpected by virtue of the early establishment of this portion of the duodenum. Its development, closely associated with that of the stomach, shows an initial preponderance over the rest of the duodenum and in the formation of its essential curves (Fig. 8).

The third stage is of the greatest importance from the point of view of errors affecting the lumen and shape of the duodenum. As already pointed out, the formation of the second and third parts of the duodenum occurs comparatively late in development, and is characterized by a period of rapid elongation eventuating in the establishment of the adult form and shape (Fig. 9). The majority of duodenal anomalies involve this portion of the gut. Any factor which interferes with this critical period of growth would lead to complete or partial obliteration of the lumen.

It would seem to us that the mechanism producing atresia, stenosis or valve formation is essentially the same, varying only in degree and in time

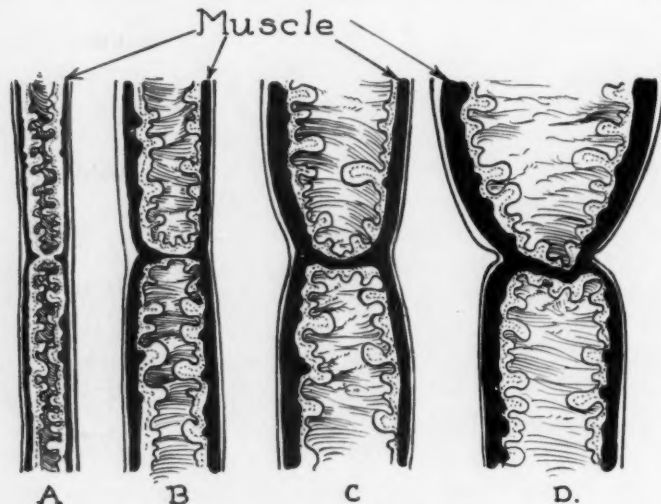


FIG. 11.—Illustrating the successive stages in the formation of a duodenal valve. Differential growth above and below the retarded area has produced the valve which therefore contains muscle between the two layers of epithelium.

of genesis. In addition, such retardation, particularly if extensive, must secondarily bring about distortion of the duodenal loop, as is so commonly found. Atresia is regarded as the result of early retardation. The same factor acting a little later would result in stenosis rather than atresia with less disturbance of the duodenal loop (Case 1). If the disturbance affects a very limited segment of the gut, differential growth above and below the point of interference would result in the formation of a valve (Fig. 11). Such a mechanism would account for the otherwise unexplained presence of muscular tissues in such septa as in Case 2. The presence or absence of septal perforation and its size may, apart from the possibility of secondary perforation, be related to the time of retardation; during, before or after the establishment of a lumen.

We regard the rapid elongation of the second and third portions as being responsible for the opening out of the duodenal loop. Anomalies of shape or retention of the primitive curve as in the duodenum in "M" may result from premature elongation before the requisite amount of space is

available for its reception or from the influence of neighboring organs such as an excessively large liver (Case 3) or premature return of the umbilical loop.

Errors of the fourth stage are the result of failure of peritoneal fixation. In themselves they are of little importance excepting insofar as they may allow of kinking of the bowel or be associated with abnormalities of rotation affecting the remaining intestine. Errors of fixation are commonly associated with obstruction of the lumen. In Case 1 a free duodenum was associated with stenosis, nonrotation of the gut, together with persistence of a hepato-duodenocolic ligament.

Diagnosis.—The past decade has added little to our store of knowledge with regard to the early diagnosis of congenital duodenal obstruction, whether due to stenosis or atresia. Ladd,³⁰ in a recent paper, again stresses the fact that duodenal obstruction will give the signs common to high intestinal obstruction. He emphasizes the importance of upper abdominal distention, visible reverse gastric peristalsis, the presence of dehydration and shock and the laboratory findings of ketosis. The afore-mentioned signs are common to all high bowel obstructions. It should be emphasized at this point that children with true hypertrophic pyloric stenosis do not vomit until the seventh or ninth day at the earliest, whereas those infants with duodenal obstructions vomit as early as the first 24 hours. Farber,¹² some five years ago, emphasized the fact that the absence of cornified epithelial cells in the meconium was proof that an atresia existed somewhere along the length of the gastrointestinal tract. He has developed a specific stain for these cells and both he and Ladd³⁰ have found that this test is of value in diagnosis. Most writers agree that hematemesis and the presence of coffee-ground vomitus in the absence of a blood dyscrasia, is a pathognomonic sign of duodenal atresia, most authors giving figures as high as from 65 to 85 per cent of all cases having this finding. Absolute constipation is the rule, but some cases pass what appears to be a true stool. Icterus of moderate degree is present in a good number of cases. One should not be misled as to the site of the atresia by the presence of bile pigments in the stool, as authors have stressed the fact that the presence of accessory biliary ducts emptying below the obstruction are not at all uncommon. The roentgenogram is, of course, of considerable value, the presence of a large gas bubble in the stomach and its site of termination often helping to confirm the diagnosis. Most surgeons attempt to corroborate their diagnosis by the giving of a small amount of barium by mouth. We feel that a warning should be posted with regard to this procedure if a later short circuiting operation is to be carried out. This warning is necessary because it has been found that the barium will often plug the anastomotic stoma, with subsequent obstruction. If barium is used it should be followed by a thorough washing out of the stomach and upper duodenum to prevent this catastrophe.

Treatment.—The treatment of congenital duodenal obstruction is essentially surgical and should be instituted at the earliest possible time compatible

with the physical condition of the infant. It is unnecessary to discuss the actual surgical procedures to be employed, except to point out that because of the smallness of the bowel in infancy, they are often attended by considerable technical difficulty. To overcome these difficulties two points with regard to surgical treatment are of special interest and deserve emphasis. The extreme contraction of the distal segment for anastomosis is one of the prime causes of trouble in performing the operative procedure and is responsible for the large percentage of postoperative complications. Clogg,⁷ as early as 1904, and Wangensteen,⁴² in 1931, have emphasized the importance of ballooning up the distal segment by means of hydrostatic pressure. This maneuver has the double advantage of increasing the size of the distal segment, thereby making it more amenable for anastomosis, and also testing the patency of the bowel lumen distal to the area of obstruction, often indicating other constrictions at lower levels which necessarily would alter the plan of procedure. Multiple constrictions are relatively common. The final point of interest, from a technical standpoint, regards the use of extremely fine silk or linen as a suture material, and the performance of the anastomosis with a single anterior and posterior layer to obviate narrowing of the lumen. It has been found that this technic rewards its user with a higher percentage of successful results. We feel that the early diagnosis of these conditions combined with prompt surgical procedure will bear fruit in giving a higher percentage of cures. A thorough knowledge of the developmental anatomy of the duodenum is essential to the diagnostic and therapeutic problems involved in the treatment of these conditions. It is perhaps the rarity of congenital obstructions which is responsible, more than anything else, for the poor prognosis in the majority of cases reported and for the relative therapeutic inertia.

SUMMARY

- (1) Three cases of congenital duodenal malformation are reported.
- (2) The literature and etiologic hypotheses are briefly discussed.
- (3) The development of the duodenum, as observed from the microscopic dissections, is given as a basis for the classification and opinions on the genesis of these anomalies.
- (4) A brief outline of diagnosis and treatment is given.

We wish to acknowledge with thanks the courtesy of the Division of Surgery, Dr. Jacob Smith for Case 2; for Case 3, Dr. Francis S. Smyth of the Division of Pediatrics; and Dr. Parry Douglas for referring Case 1.

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FURTHER OBSERVATIONS ON THE DIAGNOSIS AND TREATMENT OF GASTRIC LESIONS

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A RECENT REVIEW of the patients who were operated upon in the New York Hospital for ulcer and carcinoma of the stomach has again emphasized the difficulty of establishing a correct diagnosis of lesions of the stomach. The investigations of Bloomfield and his associates^{2, 3} of the gastric secretion have led to a better understanding of the physiology of the stomach in health and disease, and, again, have called attention to the value of gastric analysis as an aid in the correct diagnosis of gastroduodenal lesions. Their findings were corroborated by a similar study,¹ which also pointed out the difficulties experienced by the surgeon in establishing a diagnosis even when the lesion was actually visualized and palpated.

These papers dealt with lesions of the duodenum as well as of the stomach. However, since only gastric lesions present a problem in surgical therapy, so far as malignancy is concerned, it was thought that a study confined strictly to the problem of the differential diagnosis of ulcer and carcinoma of the stomach would be of value, particularly in determining the proper surgical therapy. The result of this study shows that in many instances a correct diagnosis cannot be established by any of our present methods, and is strong evidence in favor of the attitude of removal of all gastric lesions, if feasible, when surgical therapy is undertaken.

This report is based upon the findings in 53 patients with ulcer of the stomach and 104 patients with carcinoma of the stomach, who were studied thoroughly, operated upon, and followed postoperatively.

The problem of the diagnosis of gastric ulcer can best be demonstrated by referring to Chart 1, in which the comparative value of various diagnostic procedures in establishing a correct diagnosis is shown. The outstanding fact revealed is that all benign ulcers, so far investigated, have had an acidity that was normal or above normal (60 per cent free hydrochloric acid or more). During the same period 155 patients with proved duodenal ulcers were also studied, all of whom had acidities of 60 degrees or more of free hydrochloric acid.

Chart 2 lists the comparative value of the various diagnostic procedures in the correct diagnosis of carcinoma of the stomach. It will be seen that approximately a 15 per cent error in diagnosis can be expected from any

one of the diagnostic procedures. Fortunately, when all the accumulated evidence is weighed, the error in diagnosis is considerably decreased.

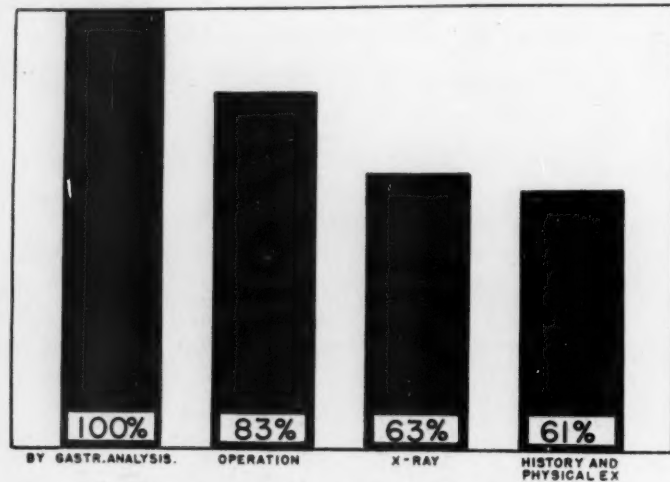


CHART 1.—Percentage of correct diagnoses in gastric ulcer.

In Chart 3 is shown the comparative value of the various diagnostic procedures in all patients with gastric lesions (ulcer 53, carcinoma 104). As appears in this chart, all available methods fail to establish a diagnosis in a certain percentage of patients. For clarity in discussion we shall consider the data in this chart separately.

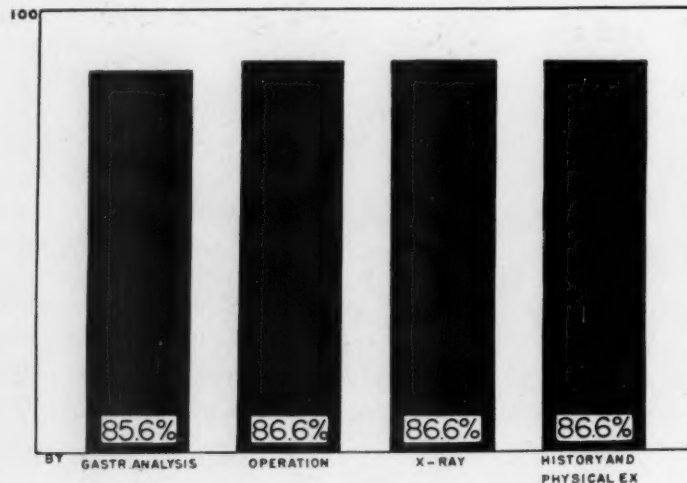


CHART 2.—Percentage of correct diagnoses in carcinoma.

History and Physical Examination.—The character and the duration of the symptoms and the age of the patient vary so greatly in ulcer and cancer that their practical value in establishing a diagnosis is minimal. Of

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greatest value is the presence of a palpable mass, which almost always signifies malignancy. Unfortunately, it is in those patients in whom the diagnosis is doubtful—whether cases of early cancer, cancerous ulcer, or ulcer—that a mass is rarely palpable. In spite of the difficulties in the differential diagnosis between ulcer and carcinoma of the stomach, a careful history and physical examination established a correct diagnosis in 61 per cent of the cases of ulcer and in 86 per cent of the cases of carcinoma.

Roentgenologic Examination.—In spite of improvements in the technic of fluoroscopy and roentgenography, the differentiation between gastric ulcer and carcinoma was not possible in 33 of 157 patients subjected to roentgenologic and fluoroscopic studies. To be sure, in the majority of instances the roentgenologist did not diagnose the lesion incorrectly, but merely stated

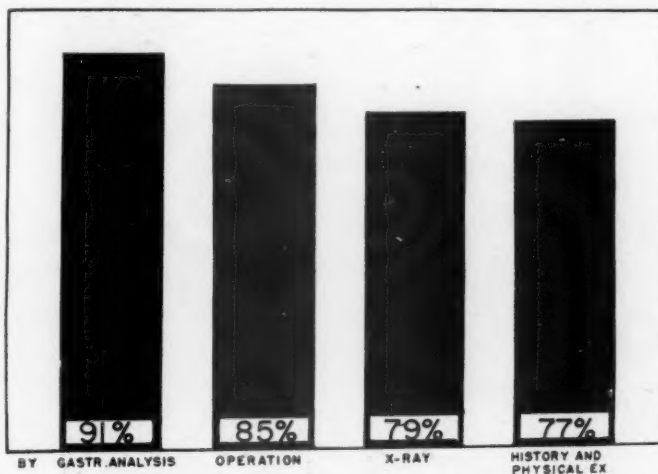


CHART 3.—Percentage of correct diagnoses in lesions (ulcer and carcinoma) of the stomach.

his inability to say definitely whether ulcer or carcinoma was present. Nevertheless, the expression of doubt by the roentgenologist in these 33 patients diminishes, for the surgeon, the value of the roentgenograms in determining the nature of the lesion.

Gastric Analysis.—Anacidity or hypo-acidity has been said to be the best evidence in favor of the presence of malignancy, and, conversely, hyperacidity to be the best evidence of benign lesions. In 15 of the 157 cases, the gastric analysis favored a diagnosis which proved to be incorrect. All these failures occurred in patients with carcinoma (104) who had 60 degrees or more of free hydrochloric acid; thus, approximately 15 per cent of patients with carcinoma have considerable acid. However, as a low acidity or an anacidity has never been found in a benign lesion, the best single evidence of malignancy is a low gastric acidity. This statement can be made only if a careful analysis, according to the method of Bloomfield and Pollard,² is made by someone who is interested in establishing the correct diagnosis. As shown

in Chart 3, the diagnosis was correct in a larger percentage of cases when it was based on the gastric analysis than when any other *single* method was relied upon.

Operative Diagnosis.—In no other part of the body do the processes of inflammation and malignancy assume such similar characteristics as they do in the stomach. In 23 of the 157 patients, the operator was unable to determine at operation, with the lesion under direct vision and palpation, whether the process was malignant or benign. In several instances an incorrect diagnosis was made. Although the majority of these patients were not operated upon by us, we had the opportunity of discussing with the surgeon his opinion and his diagnosis before he was influenced by the pathologic reports of the specimens removed.

Discussion.—First, it must be made clear that this discussion deals only with those patients in whom operative interference, for one reason or another, is contemplated. We are not suggesting rules for the treatment of all gastric ulcers, but are limiting our remarks to a consideration of the operation of choice for those patients who are about to be subjected to surgical therapy. (For discussions of the medical approach to this problem, the reader is referred to the papers of Bloomfield³ and Comfort and Van Zant.⁴) An important factor in determining the procedure of choice is whether the lesion is benign or malignant. With the exception of a low acidity or anacidity, which, when reliably determined, must be considered as an indication of malignancy, the fallibility of preoperative diagnostic criteria in the individual case is so great that their value as reliable aids is compromised, and since there is a possibility of error in diagnosis even with the lesion visible and palpable, it would seem that the treatment of choice is removal. However, considerations other than the probability of malignancy may influence the selection of a given procedure, namely, the condition of the patient, the feasibility of removal, the accessibility of the lesion, and the presence of metastases. The argument against partial gastric resection—whether wide excision or resection—because of the operative mortality, is not supported by the results in this group of patients. On 47 patients wide excisions or partial resections were performed, with three deaths, a mortality of 6.3 per cent. In conclusion it may be said that the attitude favoring removal of lesions of the stomach, when feasible, gains considerable support when confirmed by investigations on a thoroughly studied group of patients.

CONCLUSION

In summarizing, a low acidity or anacidity, determined by a reliable method, remains the single most reliable evidence of carcinoma. Since approximately 15 per cent of carcinoma are associated with considerable acid, and since all methods of diagnosis, including operative exploration, are fallible in some patients, it would seem that, when feasible, the operative therapy of choice is wide excision of the lesion or gastric resection.

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RETROGRADE ENTERIC INTUSSUSCEPTION

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RETROGRADE INTUSSUSCEPTION is a surgical entity that is infrequently seen and less often considered. Retrograde intussusception may involve any portion of the gastro-intestinal tract from the sigmoid to the stomach. In a study of the literature on this subject it is noticeable that reports of intussusception, both of the isoperistaltic and the retrograde type, have markedly increased during the past decade. It is my intention to suggest a classification and to discuss the etiology and mechanics of intussusception. The case which is herewith reported is of the enteric type and involved the ileum and jejunum.

Classification of Retrograde Intussusception.—A classification of the pathologic process along anatomic lines appears most logical: (1) Jejuno-gastric—the jejunum prolapsing through the gastrojejunostomy stoma; (2) enteric—the jejunum or ileum being involved; (3) ceco-ileal—the cecum prolapsing into the terminal ileum; (4) colic—any portion of the large bowel invaginating a more proximal part.

Numerous cases of retrograde intussusception of the jejunum as a complication of gastro-enterostomy have been noted. This is a serious sequela that may occur many years after the initial operation and may result fatally unless diagnosed early. Bettman and Baldwin⁵ reviewed the literature up to 1933, and found 33 cases similar to the one they reported. Adams¹ and Debenham¹⁰ both reported cases of retrograde jejuno-gastric intussusception with recovery. Becker⁴ records a similar case in which the intussusceptum measured 18 inches.

Cioffi⁸ and Caminiti⁷ each reported a case of retrograde intussusception involving the small intestine. The former was due to a Meckel's diverticulum while the latter was due to an angio-adenoma. Todyo,²¹ in reviewing 154 cases of intussusception, stated that he had seen three of the retrograde type. One of them was retrograde, multiple, superimposed and recurrent. Buckley⁶ operated upon a child, age two, that showed a superimposition of a retrograde upon a direct intussusception of the small intestine. D'Arcy Power,¹⁷ in 1899, wrote several accounts of the usual type of intussusception as well as accounts of his experience with two cases of the retrograde type. Clubbe,⁹ in his volume on the diagnosis and treatment of intussusception, describes a combined case of simple and retrograde intussusception. Goodyear¹³ reported one of the most interesting cases, in which he found a retrograde intussusception of the cecum into the terminal ileum. Lewis¹⁵ reported a case of retrograde intussusception of the pelvic and descending colon into the transverse colon with the apex of the intussusception at the cecum. Romanis and Mit-

chiner,¹⁰ in their text-book of surgery, record one case of retrograde intussusception in the colon of a living patient. Flemming¹² successfully operated upon an intussusception of the descending colon into the transverse colon, the etiologic factor being a benign polyp. In a study of 1,000 cases of intussusception, Fitzwilliams¹¹ reports six cases of the retrograde type. In one of them the descending colon was invaginated into the transverse colon. Schoenfeld²⁰ reported the retrograde intussusception of the sigmoid into the descending colon in a child, age four months.

Etiology and Mechanics of Intussusception.—The etiology of intussusception is still a moot question. In many instances the causal agent is evident, but in numerous instances the exact nature of the process and its inception remain a debatable problem. Perrin and Lindsay¹⁶ wrote a monograph based on a study of 400 cases. They stated that 78.5 per cent of all acute intussusceptions occur in children under two years of age. In their series they had two cases of retrograde intussusception. The following causes of intussusception were listed by them for consideration: (1) Perverted peristalsis; (2) a paralytic condition of the intestine which allowed the prolapse of one portion into another; (3) the presence of some congenital abnormality such as a constriction, or new growth such as a carcinoma, acting as the precipitating cause. They offer for further consideration the theory that the swelling of preexisting lymphoid tissue, which is especially prominent in the ileocecal region, may provoke an intussusception. In very young children gastrointestinal disturbances are quite common. When these two factors are combined, it is possible to conceive of an ileocecal or ileocolic intussusception occurring. Strong catharsis must be considered in this connection as an additional factor.

Fitzwilliams¹¹ brings out a point which is worthy of emphasis. He believes that the apex of an intussusception is fixed and does not change. During the process of invagination the apex remains as a fixed point. In discussing the mechanism further, he feels that slight intussusceptions probably form frequently but their dissolution is physiologic. In a small minority of cases it goes further. A local constriction becoming overlapped by the dilated bowel below to such an extent that it can be grasped by the latter is all that is needed to initiate an intussusception. There is a fine line between the physiologic and pathologic, and at times some small factor turns the scales.

Balfour³ has been fortunate in actually observing the mechanism of retrograde intussusception at the operating table. In an operation for obstruction due to a tumor at the sigmoid he noted that there was a retrograde intussusception of the sigmoid into the descending colon. The intussusception was reduced but as he watched the area, strong antiperistaltic activity set in and it invaginated itself again. Balfour felt that retrograde intussusception of the small intestine was an impossibility. He believes that normally there may be in the large intestine antiperistaltic contractions but does not feel that this holds true of the small intestine. He, therefore, holds that retrograde intussusception may not occur in the latter. If it does it is a terminal event

associated with simple intussusception or with the reverse peristalsis of obstruction. In reviewing the literature numerous writers quote from Lockhart-Mummery who states emphatically in his text-book: "Retrograde intussusceptions do occur but only during death or as a result of asphyxia; they are not met with in practice." This belief is contradicted by the numerous case reports in the literature of retrograde intussusception of the small intestine in the living patient. The mechanism involved is essentially the same as in the ordinary case of intussusception. Instead of having increased normal peristalsis, the neuromuscular mechanism is thrown into reverse so that forceful antiperistalsis is provoked. Alvarez² devotes an entire chapter to the subject of reverse peristalsis. He cites numerous incidents wherein drugs administered rectally were vomited some hours later. The fecal vomiting of ileus is a classic example of the reversal of normal activity.

Treatment of Intussusception.—We have traveled a long way in the matter of therapy when we consider an article written by Langstaff,¹⁴ in 1807, in which he reports a case of intussusception which ended fatally in a child, age four. He concludes: "At the same time that we recognize the inefficacy of art, these cases will teach us to repose a just confidence in the powers of nature, and to retain some hope of a favorable event under the most unpromising circumstances." Langstaff preferred to take the chance of letting the intussusceptum slough with the hope that there would be a reestablishment of the continuity of the bowel. This undoubtedly does occur since I have seen one such case in which the diagnosis was not made until after the intussusceptum sloughed and was passed per rectum. In this instance the intussusception involved the transverse and descending colon. The patient made a spontaneous recovery.

In many cases, especially in children, reduction of the intussusception has been accomplished by the use of the barium enema. However, in considering the matter of retrograde intussusception involving the large intestine, the use of the barium enema is contraindicated since all that would be accomplished would be an increase in the size of the intussusception with an aggravation of symptoms. The treatment is early and adequate surgery. The procedure to be employed will depend on the causal agent and the condition found at operation. The following case of retrograde enteric intussusception complicated by volvulus is an example of the difficulties encountered in diagnosis and the radical therapy which may be required.

Case Report.—H. R., white, female, age 69, unmarried, was seen at 7 A.M., December 29, 1938, and stated that she had been seized with a sudden, severe, spasmodic, epigastric pain, which caused her to cry out in distress. The sharp pain continued to come and go at intervals and she had continued to have a constant residual dull ache limited solely to the epigastric region. There was no radiation of pain. She was nauseated frequently and had vomited twice. Her bowels had moved that morning and there was no blood noted either in the stool or in the vomitus. Morphine sulphate was administered twice within a period of one hour with only moderate relief. She stated that she had suffered with similar episodes over a period of one and one-half years; none of these had

approached the severity of the present attack. These attacks would appear at intervals of five or six weeks and last several hours. Her last attack was five days prior to the present one.

Previous History.—Patient had been active up to ten years ago. She had had measles, mumps, whooping cough and chickenpox. There was no history of diphtheria, typhoid fever or rheumatic fever. Her tonsils and a small lipoma were removed during her childhood.

There was no history of clay-colored or tarry stools, jaundice or food intolerance. Aside from obesity she had occasional ankle edema, dyspnea on exertion, and mild arthritis. One year ago, a gastric analysis showed an anacidity, for which she had been taking 20 minims of hydrochloric acid three times a day. Ten years ago, because of easy fatigue, a basal metabolism was taken and showed -20 . She had been taking thyroid to correct this deficiency. At that time she weighed 207 pounds. Her present weight was 190 pounds. Her menopause had occurred at the age of 40.

Physical Examination.—December 29, 1938: The patient was a well developed, obese woman who appeared younger than her stated age. She looked moderately well and did not appear to be in much pain. Temperature 99.2° F. Pulse 70. Respirations 16. The heart sounds were good, with occasional extra systole. B.P. 150/80. The abdomen appeared normal in contour. No masses were seen. Palpation revealed a perfectly soft abdomen with a suggestion of tenderness in the epigastric region. There was a mass about the size of a grapefruit present in the left lower quadrant which was movable and not tender. She stated that she had been unaware of the presence of this mass. An examination by another physician, two weeks previously, had not revealed any mass.

Urinalysis showed a slight trace of albumin with a few hyaline casts. There were 2-4 R.B.C. and 3-4 W.B.C. per high power field. Hemoglobin 86 per cent, R.B.C. 4,410,000. W.B.C. 12,500, with 91 per cent neutrophils and 9 per cent lymphocytes.

Physical Examination.—December 29, 1938: The general condition of the patient remained about the same throughout the day. She was still having paroxysms of pain referred to the epigastric region but they had become less severe. She continued to be nauseated. Examination of the abdomen revealed it to be distended, especially in the left lower quadrant. It moved freely with respiration. Palpation revealed a soft abdomen. No guarding or rigidity was present. Slight tenderness was noted in the epigastric region in the midline. A large, firm, nontender, ballotable mass filled the left lower quadrant and extended two fingers' breadth above the umbilicus. It had increased materially since the earlier examination. It measured 24 cm. in length and 17 cm. in breadth. It could be grasped between the hands with ease and cause the patient no distress. The tumor was flat to percussion while the rest of the abdomen was tympanitic. W.B.C. 11,200, with 95 per cent neutrophils and 5 per cent lymphocytes. Stool examination was negative for occult blood.

Roentgenologic.—Dr. A. Petrilli, San Francisco: A. P. abdominal film: "The right kidney is readily outlined opposite the 11th and 12th dorsal and first two lumbar vertebrae. The outline of the left kidney is not definitely seen although its lower pole is suggested at approximately the same level. The right kidney appears approximately normal in size, shape and position. The general G. I. tract is unusually free of gas. Two loops of bowel containing air are seen in the left upper quadrant but it is impossible to state definitely whether these are large or small bowel. Overlying the middle of the abdomen, from the 4th lumbar vertebra to the pelvis and extending to the flanks, is a large, lobulated, soft tissue mass with smooth margins. This mass contains no air. The extension on the right side reaches to the flank but on the left it lies several centimeters from the flank. Inferiorly, it reaches the upper margin of the distended urinary bladder. The spine shows degenerative arthritic changes especially between the 4th and 5th lumbar vertebrae where the disk-space is narrowed more on the left side and there is some evidence of rupture of the nucleus pulposus. Heavy lips of bone project from the lateral margins of

these two vertebrae (Fig. 1). *Roentgenologic Diagnosis:* Intra-abdominal mass; degenerative arthritis." *Preoperative Diagnosis:* Acute intra-abdominal pathology, possibly a twisted ovarian cyst.

Operation.—Under spinal anesthesia, the abdomen was opened. There was no free fluid present in the peritoneal cavity. Several large, markedly distended, hemorrhagic and apparently gangrenous loops of bowel presented themselves. They were so apposed and adherent to each other that they gave one the impression on palpation of being a single rounded mass. The loops of bowel were gradually oriented so that it was apparent that we were dealing with a retrograde intussusception of the ileum into the ileum and jejunum as well as a volvulus at the site of intussusception. Neither the



FIG. 1.—Roentgenogram, taken three hours before operation, showing large, soft tissue mass filling the lower abdomen. The mass, outlined by dotted line, consists of obstructed bowel containing no gas.



FIG. 2.—Ileum showing multiple polypi within the lumen. (A portion of the tumor has been removed for section)

volvulus nor the intussusception could be reduced because of the extensive edema present in the bowel and mesentery. It was obvious that a resection was necessary. Seven and one-half feet of jejunum and ileum were resected and a side-to-side anastomosis performed. On opening the distal segment of bowel a small, isolated, mucosal polyp was noted. It measured approximately 2 cm. in height and 1.5 cm. at the base. It was removed for examination. The abdomen was closed without drainage. Silver wire was used as through-and-through retention sutures. Fifteen thousand units of polyanerobic antitoxin (Cutter) was administered intramuscularly.

Pathologic Examination.—*Gross:* Dr. P. M. Smith, San Francisco. "The specimen (Fig. 2) consists of approximately seven and one-half feet of small intestine; apparently it includes a small part of the jejunum, but is mostly proximal ileum. The proximal and distal two inches are pale red; the remainder is deep purplish-red and is markedly dilated, approximately 10 cm. in circumference. The mucous surface is dull red. Four point five centimeters from the proximal end, there is an abrupt line of demarcation, proximal to which the mucosa is pale and has its normal lustre. At the border of the discolored

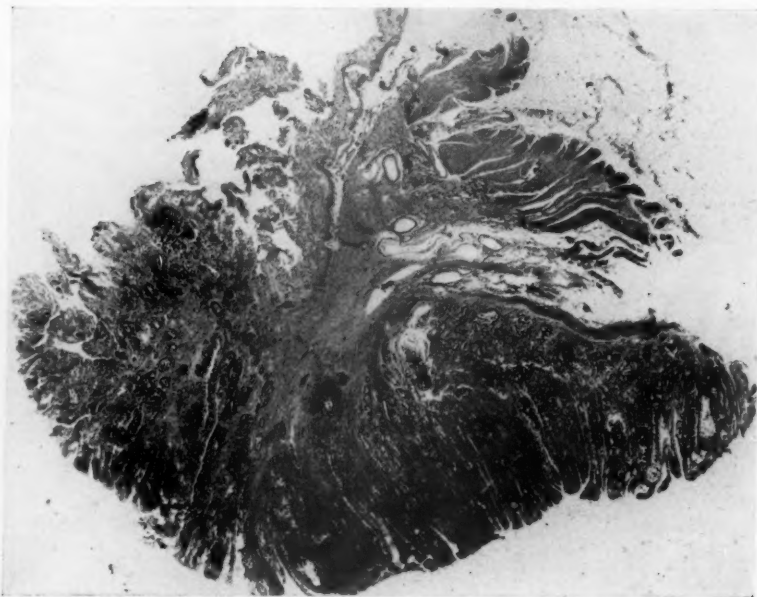


FIG. 3.—Photomicrograph of a portion of the tumor showing polyp formation.
(Low power)



FIG. 4.—Photomicrograph of the polyp: the villi are markedly elongated with the submucosa increased in thickness. The tissue is edematous, with the capillaries and veins dilated and filled with blood. (High power)

portion there is a large, irregular, flattened polypoid mass 6x6 cm. in size. The underlying wall does not seem to be infiltrated. A portion of the mesentery is markedly thickened, edematous and slightly congested. There are no thrombi in the vessels. An additional specimen measuring 1.5x1x0.5 cm. was removed from an adjacent loop of the ileum. It is partly covered by yellowish membrane."

Microscopic: "In sections from the purplish area, the tissues are edematous and the capillaries and veins are dilated and filled with blood. Many of the epithelial cells are exfoliated and their nuclei are pyknotic, but there is no loss of nuclear staining. In the polypoid masses in both the jejunum and ileum, the villi are markedly elongated and the submucosa is increased in thickness (Figs 3 and 4)." *Pathologic Diagnosis:* "Segment of jejunum and proximal ileum showing marked edema, passive congestion and dilatation. Benign mucous polypi, jejunum and ileum."

Postoperative Course:—The patient had an uneventful convalescence, her wound healing per primam. She was given three small transfusions of 250, 200, and 350 cc., and was discharged, January 26, 1939.

CONCLUSIONS

- (1) A case of retrograde enteric intussusception associated with volvulus is presented.
- (2) Retrograde intussusception may occur in any portion of the gastrointestinal tract. A classification along anatomic lines is suggested.
- (3) The diagnosis is difficult in most cases and will be made only at the time of operation.
- (4) Early surgical interference is imperative.

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DIVERTICULITIS OF THE COLON WITH SPECIAL REFERENCE TO THE SURGICAL COMPLICATIONS

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DIVERTICULA of the colon produce clinical manifestations when secondary pathologic changes of an inflammatory nature occur. These inflammatory changes may result in a variety of complications which call for surgical management. That surgical intervention in the treatment of diverticulitis of the colon is not infrequent is shown by a recent report by Brown and Marckley,² in which it is stated that, in the period from 1919 to 1929 in the Mayo Clinic, 277 cases of diverticulitis of the colon were treated medically, and 99 cases (26 per cent) were subjected to operation for this condition before or after coming to the Clinic.

The complications of diverticulitis of the colon requiring surgery may be listed as follows:

(1) Peritonitis resulting from passage of organisms through inflamed diverticula without perforation.

(2) Perforation of inflamed diverticula. In the more acute perforations varying degrees of peritonitis are present, but usually by the time perforation has occurred, protective adhesions have formed limiting the suppurative process and resulting in abscess formation.

(3) Fistula formation. Fistulae between the colon and the abdominal wall, the colon and the bladder, or the colon and another portion of the intestine may form by direct attachment and extension by necrosis, or by the secondary penetration of an abscess. There may be many submucous fistulae in the wall of the bowel.

(4) Peridiverticulitis. A chronic proliferative inflammation of the colon may occur as the result of repeated acute attacks. This chronic inflammation of the extramucosal part of the bowel wall results in a thickening of the colon with tumor-like formation, and narrowing of the lumen of the intestine. These cases may be confused with carcinoma of the colon because of the similarity in symptoms, and physical and roentgenologic findings.

(5) Metastatic suppuration.

(6) Carcinoma arising from diverticula of the colon.

Peritonitis Without Perforation of Diverticula.—One would expect a peritonitis resulting from a passage of organisms through inflamed diverticula not infrequently as it occurs in acute appendicitis, since not only is the wall of an inflamed diverticulum damaged, but it is also quite thin. However, a review of the literature gives only a few, isolated case reports. The first of these was that by Loomis,¹⁹ in 1870, who found such a condition

at postmortem examination. Other cases were reported by Cameron and Rippman,⁴ in 1910.

Peritonitis and Abscess Secondary to Diverticulitis of the Colon with Perforation.—The first case of diverticulitis of the sigmoid with perforation and diffuse peritonitis was described by Fiedler,⁹ in 1868, the condition being found at autopsy. Jaboulay,¹² in 1897, was the first to operate upon a patient with diverticulitis of the sigmoid with diffuse peritonitis. In 1911, Patel²⁶ collected from the literature 28 cases of diverticulitis of the sigmoid with perforation and peritonitis. Some of these patients were operated upon and some were not, but the condition was fatal in all.

Brewer,¹ in 1907, was the first in the American literature to report cases of diverticulitis of the sigmoid with perforation and abscess. He cited six patients who were operated upon for this condition. In the same year, Mayo, Wilson and Giffin²⁰ reported three cases of diverticulitis of the sigmoid with abscess.

Telling,²⁹ in 1908, reviewed the literature and found 50 cases of diverticulitis of the sigmoid with perforation. In 24 patients, this resulted in abscess; in 14, in diffuse peritonitis; and in one, in a perforation into a hernial sac. In 1912, McGrath²¹ stated that there were 27 patients with diverticulitis of the colon operated upon in the Mayo Clinic from 1902 to 1912. Perforation occurred in six cases, resulting in abscess formation in four of them.

Telling and Gruner,³⁰ in 1917, wrote a comprehensive article on diverticulitis of the colon, reviewing 324 cases in the literature. In this series, abscess occurred in 28 per cent (90 cases), and diffuse peritonitis in 18 per cent (58 cases). Judd and Pollock,¹⁴ in 1924, reported on the experience of the Mayo Clinic from 1907 to 1924. There had been 118 cases of diverticulitis of the sigmoid in which operations were performed. In this group, there were 17 cases of abscess, and one case of local peritonitis. There were no instances of diffuse peritonitis.

Fifield,¹⁰ in 1927, reviewed 52 cases of diverticulitis of the colon. Perforation occurred in 24 patients, resulting in abscess in 11 instances, and diffuse peritonitis in nine. In 1928, Monsarrot²² reported on 18 cases of diverticulitis of the colon. Perforation was noted in ten patients, resulting in abscess in six instances, local peritonitis in two, and diffuse peritonitis in two. In 1929, Newton²³ reviewed 44 cases of diverticulitis of the colon. Perforation occurred in 13 patients, resulting in abscess in seven, local peritonitis in one, and diffuse peritonitis in three.

Conway and Hitzrot,⁵ in 1931, reported on a series of 36 cases of diverticulitis of the colon. There were 14 instances of abscess, and nine cases of varying degrees of peritonitis. In the same year, Eggers⁷ reviewed 24 cases of diverticulitis of the colon. Perforation occurred in seven patients, resulting in abscess in three of them, and diffuse peritonitis in four. In 1934, Edwards⁶ reviewed 130 cases of diverticulitis of the colon. Perforation with peritonitis occurred in four instances, abscess in three, and abscess with secondary perforation into the peritoneum in three. Brown and Marcley,²

in 1937, reported on 88 cases of diverticulitis of the colon operated upon in the Mayo Clinic from 1919 to 1929. Perforation occurred in 17 patients, resulting in abscess in 11 instances, and varying degrees of peritonitis in six cases.

Thus, there is a great variation in the reported incidence of abscess and peritonitis resulting from diverticulitis of the colon with perforation; in the abscess group, varying from 4 to 39 per cent, and in the peritonitis group, varying from 0.8 to 25 per cent. In the entire group of 834 cases of diverticulitis of the colon, the incidence of abscess was 19 per cent, and peritonitis 12 per cent.

Fistulae.—Jones,¹³ in 1859, reported the first case of diverticulitis of the sigmoid with a fistulous communication between the bladder and the sigmoid. This was an autopsy finding. In 1907, Mayo, Wilson and Giffin²⁰ reported three cases of diverticulitis of the sigmoid which resulted in fistulae between the sigmoid and bladder. In the 50 cases of diverticulitis of the sigmoid with perforation reviewed by Telling,²⁹ in 1908, 11 patients had vesico-intestinal fistulae.

Parham and Hume,²⁵ in 1909, reviewed 385 cases of vesico-intestinal fistulae, and reported that in 65 instances the cause was inflammatory. Although only three cases of diverticulitis of the colon were noted, it is likely that this condition was also present in others of the inflammatory group, especially as in many of these the fistulae were between the bladder and the sigmoid. In the group of 27 cases of diverticulitis of the sigmoid reported by McGrath,²¹ in 1912, there were fistulous communications with the bladder in two patients.

Bryan,³ in 1916, reviewed the literature of sigmoidovesical fistulae and found that 22 of the 42 cases were secondary to diverticulitis of the sigmoid. In Telling and Gruner's³⁰ review of 324 cases of diverticulitis of the colon, in 1917, there were 38 instances of perforation into the bladder.

Sutton,²⁸ in 1921, reviewed 34 cases of vesicosigmoidal fistulae, and found diverticulitis of the colon present in six instances. In the group of 118 cases of diverticulitis of the sigmoid reported by Judd and Pollock,¹⁴ in 1924, there were eight instances of fistulae between the sigmoid and the bladder.

Fifield,¹⁰ in 1927, reported four cases of vesicocolic fistulae in a group of 52 cases of diverticulitis of the colon. In 1929, Newton²³ noted two cases of sigmoidovesical fistulae in a group of 44 cases of diverticulitis of the colon. Rankin and Brown,²⁷ in 1930, reported 48 operated cases of sigmoidovesical fistulae in a group of 481 cases of diverticulitis of the colon.

In 1932, Lett¹⁷ reported seven instances of vesicosigmoidal fistulae in a group of 172 cases of diverticulitis of the colon. Lockhart-Mummery,¹⁸ in discussion, observed four cases of sigmoidovesical fistulae in a group of 87 cases of diverticulitis of the colon. Nitch,²⁴ in discussion, stated that in 20 cases of diverticulitis of the colon, seven cases developed vesicocolic fistulae.

In a group of 130 cases of diverticulitis of the colon reviewed by Edwards,⁶ in 1934, there were two instances of fistulae between the sigmoid

and bladder. Brown and Marcle² in 1937, reported 15 cases of sigmoidovesical fistulae in a group of 88 cases of diverticulitis of the colon. Kellogg,¹⁵ in 1938, reviewed 88 cases of vesico-intestinal fistulae, and reported 37 instances of diverticulitis of the colon.

Thus, fistulae between the sigmoid and the bladder are relatively frequent complications of diverticulitis of the sigmoid, and such complications are more common in this condition than in carcinoma of the sigmoid. There is a wide variation in the reported incidence of sigmoidovesical fistulae resulting from diverticulitis of the colon, varying from 1.5 to 35 per cent, but in the entire group of 1,516 cases of diverticulitis of the colon the incidence was 8 per cent.

Peridiverticulitis.—In 1907, Mayo, Wilson and Giffin²⁰ reported five cases in which a portion of the sigmoid was excised for diverticulitis of the sigmoid with tumor-like formation and obstruction (peridiverticulitis). These were the first recorded instances in which the pathologic changes in diverticulitis of the colon were demonstrated during life. McGrath,²¹ in 1912, reported the pathologic changes of peridiverticulitis in 26 of the 27 cases of diverticulitis of the colon operated upon at the Mayo Clinic from 1902 to 1912.

Telling and Grunner,³⁰ in 1917, noted an incidence of 24 per cent (78 cases) of peridiverticulitis in their review of 324 cases of diverticulitis of the colon. In 1927, Fifield¹⁰ reported evidences of intestinal obstruction due to peridiverticulitis in 30 per cent (16 cases) of 52 cases of diverticulitis of the colon. Newton,²³ in 1929, reported two cases of large intestinal obstruction in 44 cases of diverticulitis of the colon.

In 1930, Rankin and Brown²⁷ reported an incidence of 31 per cent (71 cases) of tumefaction in 481 cases of diverticulitis of the colon. Conway and Hitzrot,⁵ in 1931, noted two cases of stenosis of the colon in a group of 36 cases of diverticulitis of the colon. Eggers,⁷ in the same year, reported nine cases with obstruction of the colon, due to a mass, in 24 cases of diverticulitis of the colon. Brown and Marcle,² in 1937, reported on 88 cases of diverticulitis of the colon operated upon at the Mayo Clinic from 1919 to 1929. In this group, 41 cases were subjected to colon resections because of the evidence of peridiverticulitis.

In the reported incidence of peridiverticulitis in cases of diverticulitis of the colon, there is a wide variation of different reports, from 6 to 96 per cent. In the entire group of 1,049 cases of diverticulitis of the colon, the incidence of peridiverticulitis was 20 per cent.

Metastatic Suppuration.—There are three reported cases of diverticulitis of the colon with metastatic suppuration, the evidences of which being found at autopsy. The first case was reported by Whyte,³¹ in 1906. His patient died of multiple liver abscesses. In 1921, Foggie¹¹ reported a case of diverticulitis of the colon with multiple lung abscesses and a brain abscess. Kramer and Robinson,¹⁶ in 1926, reported the first case of diverticulitis of the colon with pylephlebitis. This patient had a suppurative phlebitis of the mesenteric,

splenic and portal veins, a suppurative hepatitis and cholangitis, and multiple liver abscesses.

Carcinoma.—Diverticulitis of the colon bears no etiologic relationship to carcinoma of that organ. Occasionally the two conditions may coexist, but such an occurrence is incidental. This was demonstrated by Rankin and Brown,²⁷ in 1930, who reported that in 227 cases of diverticulitis requiring operation, coexisting carcinoma was found in only four instances. The same authors noted that diverticulosis of the colon was found in only four instances in a group of 679 operated cases of carcinoma of the colon. Fallon,⁸ in 1930, reported 625 cases of diverticulitis of the colon in 1,800 cases of diverticulosis of the colon. Coexisting carcinoma was found in 0.5 per cent of the cases. Diverticulitis of the colon was associated with carcinoma in 19 cases in a group of 1,600 operated cases of carcinoma of the colon.

SUMMARY OF A REVIEW OF THE LITERATURE.—Diverticulitis of the colon progressed to the development of surgical complications in over one-half of the cases, in the following incidence: Peridiverticulitis 20 per cent; abscess 19 per cent; peritonitis 12 per cent; and sigmoidovesical fistula 8 per cent.

In the ten-year period, 1927–1937, there was 35 cases of diverticulitis of the colon admitted to the Surgical Services of the Mount Sinai Hospital. There were no surgical complications in 16 of these cases. The type and incidence of surgical complications in the remaining 19 cases were as follows: Peritonitis without perforation in two; abscess in five; perforative peritonitis in five; stenosis (peridiverticulitis) in four; sigmoidovesical fistula in two; and associated carcinoma in one.

The essential features of the cases of diverticulitis of the colon without surgical complications are summarized in Table I.

The following are the case records of the 19 cases of diverticulitis of the colon with surgical complications.

PERITONITIS WITHOUT PERFORATION

Case 1.—Hosp. No. 267893: S. K., female, age 59, was admitted to the hospital, May 31, 1927, with the complaint of severe, lower abdominal pain of 12 hours' duration. There had been previous attacks of lower abdominal pain and marked constipation for 20 years. Temperature 102.4° F. There was tenderness and spasticity in both lower quadrants of the abdomen, more marked on the right side. Leukocytes 20,000, 90 per cent polymorphonuclears.

A preoperative diagnosis of acute appendicitis with local peritonitis was made, and a celiotomy was performed on the day of admission. Thin, brown, odorless fluid was found in the pelvis. There was fibrinous exudate on the wall of the sigmoid at the site of the inflamed diverticula. The appendix was removed and the pelvis drained at site of the inflamed diverticula of the sigmoid. The convalescence was uneventful, and the patient was discharged 35 days after operation.

Case 2.—Hosp. No. 276653: R. B., male, age 39, was admitted to the hospital, August 10, 1927, with a history of generalized abdominal pain for eight days, fever and obstipation for seven days, and a chill on the day before admission. The patient was acutely ill. Temperature 106.2° F. The abdomen was distended, and there was generalized abdominal tenderness and spasticity.

DIVERTICULITIS OF THE COLON

TABLE I

DIVERTICULITIS OF THE COLON WITHOUT SURGICAL COMPLICATIONS

Case	Age	Sex	History	Physical Examination	Laboratory Data	X-Ray	Course
1	66	F.	Constipation for many years; bloody diarrhea for 1 day	Temperature 100.6° F.; obesity	Hemoglobin 53%; W.B.C. 8,400, polys. 64%; gross blood in stools	Multiple, large diverticula and marked spasticity of entire colon	Improved; recurrence of bloody stools 2 yrs. later; died 4 yrs. later—cause unknown
2	83	F.	Upper abdominal pain for 2 wks.; constipation for 10 days	Temperature 101° F.; obesity	W.B.C. 8,200, polys. 73%	2 diverticula and marked spasticity of sigmoid	Improved
3	66	F.	Constipation for 10 yrs.; epigastric pain for 3 yrs.; loss of weight for 8 mos.	Temperature 100.4° F.	W.B.C. 5,600, polys. 50%	Many diverticula in descending colon and sigmoid, with marked spasticity of sigmoid	Improved; symptom-free 6 mos. later
4	72	F.	Upper abdominal pain, nausea, vomiting and abdominal distention for 2 yrs.; marked upper abdominal pain and constipation for 3 days	Temperature 102° F.; generalized abdominal tenderness and distention; obesity	W.B.C. 23,900, polys. 91%	Several large diverticula and marked spasticity of sigmoid	Improved; occasional abdominal pain 3 yrs. later
5	67	M.	Lower abdominal pain and constipation for 5 days	Temperature 99.6° F.; mass in left lower quadrant of abdomen	W.B.C. 14,000, polys. 87%	Many diverticula and spasm of sigmoid	Improved; died 3 yrs. later—cause unknown
6	68	M.	Lower abdominal pain and constipation 10 yrs. ago, and for past 8 days	Temperature 101.6° F.; tenderness in lower left quadrant of abdomen	W.B.C. 16,000, polys. 81%	Several, small diverticula and spasm of sigmoid	Improved
7	57	F.	Constipation for many years; abdominal pain for 3 days	Temperature 100.4° F.; tenderness in left lower quadrant of abdomen	Guaiac positive stool	Several, small diverticula of sigmoid	Improved
8	76	F.	Diarrhea for 13 yrs.; abdominal pain for 2 yrs.	Temperature 100° F.; obesity	W.B.C. 9,100, polys. 78%	Diverticula of sigmoid, with marked spasm of descending colon and sigmoid	Improved; symptom-free 1 yr. later
9	66	F.	Generalized abdominal pain and diarrhea for 3 wks.	Temperature 100.2° F.; sigmoidoscopy negative	W.B.C. 6,300, polys. 58%	Diverticula of ascending and descending colon and sigmoid, with moderate spasm of sigmoid	Improved
10	64	M.	Constipation 1 mo.	Temperature 103° F.; sigmoidoscopy negative	W.B.C. 30,800, polys. 82%; guaiac positive stool	Many diverticula and spasm of descending colon	Improved

TABLE I (Continued)

Case	Age	Sex	History	Physical Examination	Laboratory Data	X-Ray	Course
11	76	F.	Diarrhea and loss of weight for 8 mos.	Temperature 100.6° F.; spasm at rectosigmoid on sigmoidoscopy	Guaiaec positive stool	Diverticula and spasm of sigmoid	Improved; recurrence of diarrhea 4 yrs. later
12	77	M.	Constipation for many years; generalized abdominal pain and loss of weight for 3 mos.	Temperature 99.2° F.; sigmoidoscopy negative	Guaiaec positive stool	Diverticula of hepatic flexure, descending colon and sigmoid, with marked spasm of descending colon and sigmoid	Improved
13	78	M.	Abdominal pain and constipation for 3 days	Temperature 104° F.; tenderness in right upper quadrant of abdomen; abdominal distention	W.B.C. 8,000, polys. 80%	Many diverticula and spasm of descending colon and sigmoid	Improved
14	70	F.	Diarrhea and vomiting 6 and 3 yrs. ago; diarrhea; upper abdominal pain, and loss of weight for 3 mos.	Temperature 100.2° F.; marked spasm and injection of mucosa of sigmoid on sigmoidoscopy	W.B.C. 6,200, polys. 72%	Many small diverticula and spasm of sigmoid; diverticulum of second part of duodenum	Improved
15	64	F.	Pain in left lower quadrant of abdomen and blood in stool for 2 days	Temperature 102° F.; tenderness in left lower quadrant of abdomen	W.B.C. 19,000, polys. 84%	Many small diverticula and spasm of sigmoid	Improved
16	50	F.	Lower abdominal pain for 2 days	Temperature 100.4° F.; tenderness and spasm in left lower quadrant of abdomen	W.B.C. 11,300, polys. 60%	Diverticula of descending colon and sigmoid, with spasm of sigmoid	Improved

A preoperative diagnosis of acute appendicitis with diffuse peritonitis was made, and a celiotomy was performed on the day of admission. A diffuse peritonitis was found, and an appendicectomy and drainage was performed. The patient died five hours after admission. The culture of the peritoneal fluid was reported *Streptococcus haemolyticus*.

Autopsy.—The peritoneum was dull and covered by fibrinous exudate, with about 200 cc. of sanguinopurulent fluid in the peritoneal cavity. The peritonitis was most marked in the pelvis. Some coils of lower ileum were lightly adherent to the sigmoid. The sigmoid was found to be markedly indurated and adherent to the posterior peritoneum. The regional lymph nodes of the sigmoid were enlarged. When opened, the colon showed numerous inflamed, narrow-mouthed diverticula extending from the ascending colon to the sigmoid.

PERFORATION WITH ABSCESS

Case 3.—Hosp. No. 265596: R. M., male, age 38, was admitted to the hospital, March 29, 1927, with the complaint of pain in the left lower quadrant of the abdomen and left

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flank of three days' duration. Temperature 102.6° F. There was tenderness in the epigastrium, and tenderness and spasticity in the left upper quadrant of the abdomen. Leukocytes 18,000, 86 per cent polymorphonuclears.

During the first week of hospitalization, the patient ran a temperature from 101° to 103.8° F. The abdominal signs and leukocytosis continued. Clinical and roentgenologic evidences of a consolidation of the lower left lobe developed. Tenderness over the left lower ribs was noted. The patient was thought to have a left subphrenic abscess, and he was operated upon one week after admission. A large abscess under the left diaphragm, mesial and lateral to the spleen, was incised and drained.

Postoperative Course.—The patient ran a stormy course. Elevated temperature continued for about two months. A fecal discharge was noted from the wound soon after operation and persisted for five weeks. There were persistent clinical and roentgenologic signs of a pneumonia of the left lower lobe. A barium enema, two months after operation, revealed a large diverticulum in the upper portion of the descending colon with considerable spasm of the entire descending colon. The tip of a drainage tube was close to the site of the diverticulum. The patient was discharged two months after admission.

Subsequent Course.—The patient was readmitted four years later, with a history of lower abdominal pain and fever of three days' duration. Temperature 104° F. There was tenderness and spasticity in the left lower quadrant of the abdomen. Leukocytes 18,200, 82 per cent polymorphonuclears.

The temperature dropped steadily, and was normal by the fourth day of hospitalization. By this time, the abdominal signs had disappeared, and the leukocytes were normal. During the second week of hospitalization a mass was felt in the left lower quadrant of the abdomen. The patient was discharged three weeks after admission.

The patient remained well for a period of four years, when he was again readmitted because of pain in the epigastrium and upper right quadrant of two days' duration. There was tenderness in right upper quadrant, and a roentgenogram of the gallbladder showed failure of visualization. A cholecystectomy for chronic cholecystitis and cholelithiasis was performed. The patient's convalescence was uneventful.

Case 4.—Hosp. No. 295313: J. G., male, age 55, was admitted to the hospital, October 3, 1928, with the history of a chill ten days previously. This was followed on the next day by pain in the lower abdomen in the midline, and on the left side, which continued until admission. For five days the patient had had chills and had run a temperature up to 104° F. Thereafter the chills stopped, but the temperature continued.

On admission, the temperature was 102° F. There was marked tenderness in the left lower quadrant of the abdomen. On rectal examination there was a small, tender mass high up on the left side. Leukocytes 5,200, 68 per cent polymorphonuclears. Barium enema showed spasm of the sigmoid. The patient continued to have an elevated temperature up to 101.6° F. for two weeks.

Operation.—Two weeks after admission: Spinal anesthesia. The sigmoid was bound down to the bladder anteriorly, the small intestine mesially, and the lateral pelvic wall laterally. On separating the sigmoid from the lateral pelvic wall, an abscess was encountered containing two ounces of thick, creamy, odorless pus. The sigmoid and its mesentery in this region felt indurated, and the operator was in doubt as to whether this induration was due to neoplasm or inflammation. On the anterior and lateral walls of the sigmoid there were multiple diverticula, and on the posterior wall a perforation could be seen which entered the mesentery. After the abscess was evacuated, the mesosigmoid was ligated, and a Mikulicz exteriorization of the sigmoid was performed, draining the mesentery on either side with packing and rubber dam. A tube was placed in the pelvis. The culture of the pus was reported *B. coli*.

The exteriorized sigmoid was found to be necrotic, and was excised two days after operation. Clinical evidences of peritonitis developed, and the patient died two weeks after operation.

Autopsy.—There was a gangrenous inflammation of the abdominal wound and tissues surrounding the operative site with localized pelvic peritonitis. There were many inflamed diverticula of the sigmoid.

Case 5.—Hosp. No. 345651: P. K., male, age 57, was admitted to the hospital, November 14, 1932, with a history of right lower quadrant abdominal pain, constipation, and vomiting of four months' duration, loss of weight for two months, and a chill two weeks before admission, with continuous fever since then. Temperature 98.6° F. Examination of the abdomen showed slight tenderness in the right upper quadrant. Barium enema revealed spasm and many diverticula of the sigmoid. On the twelfth day of hospitalization the stools became grossly bloody. Two days later there was a rise in temperature to 103° F., associated with lower abdominal pain and bloody stools. Rectal examination revealed a mass on the left side extending upward. On sigmoidoscopy, there was found to be an obstruction at the rectosigmoid, with a polypoid appearance of the mucosa at that site.

Operation.—Seventeen days after admission: Spinal anesthesia. The sigmoid was found to be rather short and fixed. Several diverticula of the sigmoid were seen. An abscess, posterior to the sigmoid, was entered and about two ounces of thick, creamy, odorless pus was evacuated. A rubber tube drain was inserted into the abscess cavity. The culture of the pus was reported *B. coli*.

The patient's postoperative course was uneventful except for some wound infection until the tenth day, when the temperature rose to 104° F., and he died 36 hours thereafter.

Autopsy.—There was an inflammatory mass involving the sigmoid, omentum and a loop of ileum in which there were a number of small abscesses containing green pus. The descending and sigmoid colon was adherent to the lateral parietal peritoneum. The abscess to the left of the sigmoid had been drained. From the abscess cavity, a probe could be inserted through a small perforation into the lumen of the sigmoid at the site of a perforated, inflamed diverticulum. At the site of attachment of the ileum to the sigmoid, there was an ileosigmoidal fistula. The wall of the sigmoid was greatly indurated. The mucosa was thickened, reddened and granular. There were many diverticula of the sigmoid, the mouths of which were patent but narrow. Most of the diverticula contained fecoliths.

Case 6.—Hosp. No. 406338: C. R., female, age 38, was admitted to the hospital, March 27, 1937, with the history of chills and fever starting 16 days before admission. The following day she began to complain of left lower quadrant abdominal pain which persisted until admission. Associated with the onset of the abdominal pain, there was severe, nonbloody diarrhea which lasted for three days. The patient vomited several times during the first two days of her illness. The chills and fever subsided after the first day of the illness, but recurred daily for three days prior to admission. Temperature 103.2° F. Examination revealed a large, hard, tender mass in both lower quadrants of the abdomen, more on the left side, extending to the umbilicus. There was tenderness and spasticity in both lower quadrants of the abdomen away from the mass, more on the left side. Pelvic examination revealed a hard, nodular mass in the pelvis. Leukocytes 18,700, 80 per cent polymorphonuclears. The temperature continued to be elevated, the mass became larger, and the patient's general condition became worse. On the third day of hospitalization, the temperature rose to 105.2° F.

Operation.—Three days after admission: Avertin-gas-oxygen-ether anesthesia. There was some clear, yellow fluid in the peritoneal cavity, with dilatation of the small intestine. A large, hard mass occupied almost all of the left lower quadrant. The sigmoid was separated from the lateral pelvic wall, and an abscess was entered containing about two ounces of thick, foul-smelling, green pus and air. The abscess was drained by tube and packings. The patient's condition remained poor and she died during the first postoperative day.

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Autopsy.—In the pelvis, especially on the left side, there were an adherent series of ileal loops to a large mass, the size of a grapefruit. The rubber tube drain and packings entered a bilocular abscess cavity, each locule measuring about 7x5 cm. in diameter. The walls of the cavities were lined by a thick, rough, shaggy, green exudate, and in one locule there was about 200 cc. of turbid, thin, green, foul-smelling fluid. The other locule was empty. The abscess cavity was bounded by the bladder anteriorly, the uterus mesially, the left broad ligament and the sigmoid posteriorly, and the pelvic peritoneum and sigmoid laterally. An undrained abscess cavity was found posteriorly behind the left broad ligament, between it and a pedunculated fibroid arising from the posterior wall of the uterus. The cavity was about 6x4 cm. in diameter, was not connected with the anterior drained abscess, and contained about 100 cc. of thin, green, foul-smelling fluid. The wall of the sigmoid was thickened. The serosal surface formed a part of the lateral wall of the large, anterior abscess. Three diverticula were found in the sigmoid. Two of these were perforated, entering the anterior and posterior abscesses, and the third was intact.

Case 7.—Hosp. No. 415178: F. C., male, age 35, was admitted to the hospital, October 9, 1937, with the complaint of lower abdominal pain of eight days' duration. The pain had gradually decreased in severity until the day before admission, when it became severe following an enema. During the same period he had nausea and an intermittent temperature up to 102° F. He had always been constipated. Temperature 102.8° F. On rectal examination a tender exudate was felt high up. Leukocytes 22,100, 89 per cent polymorphonuclears.

The patient was given intravenous fluids for a week, and during this period a Levin tube was used to combat abdominal distention. During this time, the temperature ranged from 99.4° to 103.4° F. The leukocytes dropped to 13,700, with 80 per cent polymorphonuclears. At the end of the first week of hospitalization, the rectal exudate was less, the tenderness decreased, and the spasticity had disappeared. During the second week of observation, the rectal mass became smaller, and an indefinite mass was felt in the lower abdomen. The temperature ranged between 99.2° and 102° F.; leukocytes 12,400, with 80 per cent polymorphonuclears. During the third week, the rectal mass could not be felt, and the abdominal mass was still questionable. The temperature varied between 99° and 101.8° F.; leukocytes 11,900, with 83 per cent polymorphonuclears. During the fourth week, the mass in the lower abdomen was distinctly palpable.

Operation.—Five weeks after admission: Avertin-gas-oxygen-ether anesthesia. A pelvic abscess was found which contained about six ounces of thick, green, odorless pus. The appendix was not acutely inflamed. The abscess was drained with Penrose drains. The culture of the pus was reported *B. alkaligenes*. A fecal fistula was noted one week postoperative, which lasted for two weeks. A low grade fever continued until discharge. The patient left the hospital three weeks after operation.

Subsequent Course.—A barium enema performed three months after discharge revealed diverticula and spasm of the sigmoid. The patient was symptom-free for a period of 16 months, when he was readmitted with the complaint of lower abdominal pain of four days' duration. The examination was negative except for a ventral hernia at the operative site. Sigmoidoscopy was negative, and the barium enema revealed the diverticula and spasm of the sigmoid. The abdominal pain soon subsided and the patient was discharged in ten days.

PERFORATION AND PERITONITIS

Case 8.—Hosp. No. 277092: Baby S., male, age 18 hours, was admitted to the hospital, February 25, 1927, with abdominal distention, obstipation and vomiting since birth. The child was full term, and there was nothing unusual about the delivery. Temperature 100° F., and the abdomen was markedly distended.

Operation.—Two hours after admission: Ether anesthesia. The peritoneal cavity was filled with dark brown fluid. The small intestines were distended, purple in color,

and covered by fibrinous exudate. An ileostomy was performed. Following operation, the child's condition remained poor, and he died three days after operation.

Autopsy.—The peritoneal cavity contained about 50 cc. of brown fluid. The peritoneum and peritoneal surfaces of the abdominal organs were coated with a fibrinous exudate which assumed a plastic character in the upper abdomen, especially over the liver, omentum and spleen. The enterostomy tube was found in the ileum, about 15 cm. above the ileocecal valve. The small intestine proximal to this was moderately distended. The remainder of the ileum and the large intestine were collapsed. The omentum was rolled up and lay in the left upper quadrant. It was greenish-black in color, and in attempting to separate it from the surrounding adherent structures, it was found to enclose a large abscess cavity. There was an inflamed, perforated diverticulum of the splenic flexure of the colon, which opened into the abscess cavity.

Case 9.—Hosp. No. 288489: M. R., female, age 71, was admitted to the hospital, February 25, 1928, with the history of generalized abdominal pain and obstipation for two days, and vomiting for one day. Temperature 103° F. The abdomen was distended, and there was generalized abdominal tenderness and spasticity. Leukocytes 8,600, 96 per cent polymorphonuclears. Soon after admission, the pulse became very irregular, and there was marked circulatory collapse. The patient's poor condition continued, and she died one week after admission.

Autopsy.—The peritoneal cavity contained about 300 cc. of yellow pus and fibrin. There was a large diverticulum, about 2 cm. in diameter, in the duodenum just below the papilla of Vater. In the cecum there were three small diverticula. There were several small diverticula of the sigmoid, one of which had perforated. The sigmoid wall was necrotic around the perforated area.

Case 10.—Hosp. No. 348476: E. M., female, age 44, was admitted to the hospital, January 29, 1933, with the history of lower abdominal pain following the taking of Epsom salts, vomiting and diarrhea of three days' duration, and a chill one hour before admission. Temperature 104.4° F. There was a diffuse abdominal tenderness and spasticity, most marked in the left lower quadrant. In the latter region, a large indefinite mass could be felt.

Operation.—Four hours after admission: Spinal anesthesia. The peritoneal cavity contained free, turbid fluid. Loops of bowel and omentum were adherent in the region of the sigmoid, forming a large mass which extended down into the pelvis. The small intestine was congested, dilated, and covered with flakes of fibrin. Thick pus was found in the pelvis. Two small necrotic areas were found on the anterior wall of the sigmoid. This loop of the sigmoid was exteriorized, and the abdomen was drained. The patient's condition remained poor, and she died during the first postoperative day.

Autopsy.—The exteriorized loop of sigmoid was dark red in color and presented an opening about 4 Mm. in diameter into its lumen. There was seropurulent fluid in the pelvis, in both lumbar gutters, and under the liver. Several collections of thick, green pus were found between intestinal loops. The intestines were markedly dilated. The descending colon and sigmoid showed many diverticula, two of which in the sigmoid had perforated.

Case 11.—Hosp. No. 375348: R. S., male, age 28, was admitted to the hospital, January 5, 1935, with the complaints of para-umbilical pain and nausea of 14 hours' duration. He vomited and had a chill one hour after onset of the pain. He had had two previous attacks of abdominal pain, one seven months and the other six weeks before. Temperature 103.4° F. There was marked tenderness and spasticity in both lower quadrants of the abdomen. On rectal examination, there was tenderness and fullness high up. The preoperative diagnosis was acute appendicitis with local peritonitis.

Operation.—Three hours after admission: Gas-oxygen-ether anesthesia. The peritoneal cavity contained a large amount of thin, greenish-yellow fluid. The appendix was not acutely inflamed. The loops of small intestine in the pelvis were reddened. There was a small amount of fibrin on the sigmoid. A small, necrotic area with an

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obvious perforation was found in the wall of the sigmoid near the mesenteric attachment. Two fatty beads presented close to the area of perforation. The perforation was closed, and drainage instituted to the site of perforation.

The culture of the pus was reported *B. coli*. The postoperative course was uneventful. Intravenous fluids were given for three days. The temperature was normal by the fifth postoperative day. The patient was discharged on the fifteenth postoperative day.

Case 12.—Hosp. No. 389034: S. H., male, age 49, was admitted to the hospital, January 20, 1936, with the history of lower abdominal pain, constipation, vomiting and fever of six days' duration. Temperature 99.2° F. There was generalized abdominal tenderness and spasticity. On rectal examination a firm, tender mass was felt on the left side. Leukocytes 8,600, 69 per cent polymorphonuclears. The temperature rose to 103.6° F. 16 hours after admission. The leukocytes were 20,800, 90 per cent polymorphonuclears, on the second day of hospitalization. The patient's condition steadily grew worse, the temperature ranging between 103° and 105° F. His condition was felt to be too poor for surgical intervention. The patient died on the fifth day of hospitalization.

Autopsy.—The peritoneal cavity contained about 500 cc. of thick, gray, purulent fluid, much of which was accumulated in many locules between loops of intestine. There were large collections of purulent fluid beneath the liver, in the right lower quadrant and in the pelvis. The loops of small intestine were distended, discolored and adherent to each other. The omentum was adherent to the sigmoid. The colon was moderately dilated. The sigmoid and the distal third of the transverse colon presented about ten diverticula, some of which were filled with inspissated fecal material. There was one large diverticulum about 1 cm. in diameter, in the posterior wall of the sigmoid, 5 cm. proximal to the rectosigmoid. This opened into a cavity 3 cm. in diameter, the walls of which were formed by the sigmoid and retroperitoneal tissues. From here, a tract ran posteriorly and mesially into the peritoneal cavity. The serosa of the sigmoid and the proximal 10 cm. of rectum were thickened.

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Case 13.—Hosp. No. 256430: M. C., male, age 48, was admitted to the hospital, January 25, 1927, with the history of constipation, and difficulty in starting the urinary stream of two weeks' duration. Physical examination was negative except for a mass felt on rectal examination. Sigmoidoscopy and barium enema revealed an obstruction in the sigmoid.

Operation.—The sigmoid was found to be bound down in the pelvis by dense adhesions. About two inches of the sigmoid were involved in a dense, hard mass, feeling like carcinoma. This region of the sigmoid was excised, and a side-to-side anastomosis was performed. Examination of the specimen showed a thickened wall of the sigmoid, with the mouths of several diverticula seen in the mucosa. There was no evidence of malignancy. The patient's convalescence was complicated by multiple neuritis. The patient was discharged well six weeks after operation.

Case 14.—Hosp. No. 285674: I. K., male, age 73, was admitted to the hospital, November 25, 1927, with the history of obstipation and abdominal distention for two weeks, and generalized abdominal pain for five days. Temperature 101.4° F. There was marked abdominal distention, and some generalized abdominal tenderness and spasticity. The patient refused operation, and died the next day from circulatory failure.

Autopsy.—There was a marked distention of the colon. The sigmoid was collapsed and adherent to the posterior parietal peritoneum. A firm tumor mass was felt in this region of the sigmoid. The visceral peritoneum was reddened, and the peritoneal cavity contained about 300 cc. of brownish, cloudy fluid. There were many small diverticula filled with fecal material in the descending colon. The sigmoid was markedly stenosed. There were many diverticula in the sigmoid which penetrated the muscular layer and

extended into the underlying fat tissue. The muscular layer of the sigmoid was very hypertrophied. There were several small ulcerations in the dilated cecum.

Case 15.—Hosp. No. 315672: J. L., male, age 54, was admitted to the hospital, June 21, 1930, with the history of a painful swelling in the left lower quadrant of the abdomen and diarrhea of six months' duration. Temperature 99.4° F. There was an elastic, tender, egg-sized mass in the left lower quadrant of the abdomen. The stool was guaiac positive and purulent. Leukocytes 8,800, 84 per cent polymorphonuclears. Sigmoidoscopy showed an obstructing mass at the rectosigmoid, covered by inflamed mucosa and a purulent membrane. A biopsy from the region was reported chronic and acute inflammation. A barium enema showed a marked spasticity of the sigmoid. There were many diverticula of the colon extending from the cecum to the sigmoid. One of the diverticula, at the junction of the descending colon and sigmoid, extended about one-half inch extraluminally.

Operation was advised, but the patient refused and left the hospital. He died five years later. The cause of death was not known.

Case 16.—Hosp. No. 321003: J. C., male, age 65, was admitted to the hospital, December 6, 1930, with the history of frequency of urination and dysuria of one month's duration. Rectal examination revealed an enlargement of the prostate. Pus and red cells were found in the urine. Temperature 98.6° F. Leukocytes 8,600, 70 per cent polymorphonuclears. Cystoscopic examination disclosed an enlargement of the middle lobe of the prostate, and a suprapubic cystotomy was performed, in the course of which an extravesical mass was felt through the posterior wall of the bladder. Because of this finding, attention was directed to the colon. Sigmoidoscopy demonstrated an intussusception of the sigmoid into the rectum which made the examination unsatisfactory. A barium enema showed a marked delay to the passage of the barium at the distal portion of the sigmoid about eight inches from the anus. The barium progressed along a constricted position for distance of about one inch. With more pressure the obstruction was partially overcome.

Operation.—Spinal anesthesia. A large mass in the region of the rectosigmoid was found. The mass was densely adherent to the bladder and between the two there was a small perisigmoidal abscess. The lesion was considered to be a carcinoma. The mass was excised, and an end-to-end anastomosis of the divided ends of the sigmoid was performed. The pathologic report was diverticulitis and perisigmoiditis. The patient died one week after operation. There was no autopsy, but there were clinical evidences of peritonitis.

SIGMOIDOVESICAL FISTULA

Case 17.—Hosp. No. 334704: A. R., male, age 39, was admitted to the hospital, July 27, 1929, with a left inguinal hernia of seven months' duration, and diarrhea and hematuria of three months' duration. His Wassermann was four plus, and he was given antiluetic therapy. He was readmitted four months later, with the history of urinary frequency and dysuria, vomiting and chills of four months' duration. No cause was found for these symptoms. Four months later, the left inguinal hernia was repaired. He was readmitted two years later, with the history of bloody diarrhea, abdominal pain, weakness and loss of 20 pounds in weight of three months' duration. There was a firm, tender mass in the left lower quadrant of the abdomen. On sigmoidoscopy, the rectal mucosa was found to have a granular appearance. A biopsy of this tissue was reported granulation tissue with chronic inflammation. A barium enema showed a partial obstruction in the region of the midsigmoid. Some barium was able to pass this region into the descending colon which appeared dilated. There was considerable spasticity and many diverticula of the sigmoid. While under observation, the patient had recurrent attacks of abdominal pain, and in one of these the leukocytes were 25,000, 88 per cent polymorphonuclears. Under conservative therapy the patient's symptoms subsided.

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The last admission was January 27, 1932, two months after the previous one. During this period he continued to have diarrhea and dysuria. There was a hard, slightly tender mass in the left lower quadrant of the abdomen. On sigmoidoscopy, the granular appearance of the rectal mucous membrane was again noted. The stool contained a mixture of mucus and blood. Leukocytes 8,800, 54 per cent polymorphonuclears. While under observation, the patient was noted to pass gas from the urethra during urination. On cystoscopy, an edematous, polypoid mass covered by exudate was found on the posterior wall of the bladder. A fistula in this region could not be demonstrated.

Operation.—Spinal anesthesia. The lower sigmoid and rectosigmoid were found to be the site of an inflammatory mass which bound them to the posterior wall of the bladder. A sigmoidovesical fistula was demonstrated, and the openings in the sigmoid and bladder were closed. The sigmoid was markedly thickened and edematous. The diseased sigmoid, about 15 cm. in length, was excised, and an end-to-end anastomosis of the cut ends of the sigmoid was performed, followed by a tube cecostomy. Examination of the specimen showed the wall of the sigmoid to be white, firm and cartilaginous in consistency, with some polyposis of the mucous membrane. Three diverticula were found. The pathologic report was chronic diverticulitis with fibrosis and perisigmoidal acute and chronic inflammation. The patient died five days after operation with clinical evidences of peritonitis.

Autopsy.—The site of the end-to-end anastomosis of the sigmoid, except for a few sutures, was open posteriorly. The distal margin of the anastomosis and the lower 6 cm. of the rectum were blackish-red in color and showed a number of shallow, irregular ulcerations. The intervening mucosa, although dark in color, was not necrotic. The bladder wall was thickened. Sutures were present in the posterior wall of the bladder. On the posterior aspect of the fundus a mouth of a sinus tract was found which led to the sutured area posteriorly. The small and large intestines were distended and adherent to each other by fibrinous exudate. There was a moderate amount of sero-purulent fluid in the peritoneal cavity.

Case 18.—Hosp. No. 346502: M. S., male, age 59, was admitted to the hospital, December 7, 1932, with a history of frequency of urination and dysuria of six years' duration. For three weeks prior to admission, these symptoms had become more marked, the patient passing thick, bloody urine every hour. The patient's bowel movements were fluid in character, and for three weeks preceded each voiding. Temperature 101° F. On rectal examination, there was a large area of induration extending upward from the left lobe of the prostate. The patient was passing grossly purulent and bloody urine. Blood urea 34 mg. per 100 cc. A roentgenogram of the urinary tract showed a large number of irregular concretions in the region of the symphysis pubis, which were interpreted as prostatic calculi.

In view of the grossly purulent urine, it was felt that any attempt to catheterize the patient would be followed by an epididymitis. Accordingly, a section of the vas deferens on both sides was performed. On the day following this procedure, the patient stated urine came through the rectum. On further questioning, he stated that he had passed urine from the rectum for a month prior to admission. A catheter was passed and methylene blue was injected into the bladder. The dye was seen in the rectum through a proctoscope. The exact site of vesicorectal communication could not be seen.

A suprapubic cystotomy was performed, 12 days after admission. The bladder contained thick, brown fluid and pieces of necrotic tissue. The prostate was enlarged and contained small calculi. The bladder was drained. Just prior to operation, the patient appeared quite ill. The abdomen was distended and the pulse 150. The clinical picture suggested a peritonitis. Following the suprapubic cystotomy his general condition improved, although the abdominal distention persisted. On sigmoidoscopy, an obstruction was met about 15 cm. from the anus. In view of the persistent abdominal distention, a transverse colostomy was performed under local anesthesia. The ascending, transverse and descending colon were greatly dilated. Following the colostomy, the tempera-

ture continued from 101° to 104° F., the pulse ranged from 130 to 150, but the abdominal distention was relieved. He drained about 1,500 cc. of thick, dark urine from the suprapubic tube daily. Three days after the colostomy, the patient presented the picture of beginning uremia, with twitching of the extremities. The blood urea, which had come down to 15 mg. per 100 cc. after the suprapubic cystotomy, rose to 40 mg. The patient died four days after the colostomy.

Autopsy.—Upon opening the sigmoid, an obstruction was found about ten inches proximal to the rectosigmoid junction. Here the wall of the sigmoid was markedly thickened. The sigmoid was firmly attached at this point to the underlying structures. At the rectosigmoid, the wall of the bowel was again thickened and the lumen stenosed. There was multilocular abscess which extended along either side of, and posterior to, the sigmoid, and continued down around the rectum, so that the rectum lay as an isolated tube in the midst of an abscess. The abscess involved the perisigmoidal and perirectal tissues, and communicated with the fundus of the bladder by an opening about 2 cm. in diameter, and with the prostate by a sinus through the periprostatic tissues. The walls of the abscess were necrotic. At the point of marked obstruction of the sigmoid there were many diverticula, a few of which had perforated into the large perisigmoidal abscess. The other findings were a gangrenous cystitis, ascending pyelonephritis, chronic peritoneal adhesions, and tension ulcers of the ileum and cecum.

CARCINOMA ASSOCIATED WITH DIVERTICULITIS

Case 19.—Hosp. No. 379596: A. H., female, age 65, was admitted to the hospital, May 8, 1935, with the history of left lower quadrant abdominal pain of 20 years' duration, and diarrhea of seven years' duration. The pain had been severe for eight days prior to admission. The patient had been in the hospital three years before, at which time a diverticulosis of the colon had been demonstrated. Temperature 101.8° F. The abdomen was distended and there was a firm, tender mass in the left lower quadrant. On rectal examination, a hard, tender mass could be felt extending up the left pelvic wall. Leukocytes 23,200, 92 per cent polymorphonuclears. The patient was treated conservatively for two weeks, during which time the pelvic mass, felt on rectal examination, grew larger.

Operation.—Gas-oxygen-ether anesthesia. A large abscess in the left lower quadrant of the abdomen was found and drained. The patient died two days after operation.

Autopsy.—The peritoneum in the lateral gutters, from the pelvis to the diaphragm, was covered by a fibrinous exudate, and filled with turbid fluid. Pockets, produced by adhesions of loops of small intestine, were filled with the same character of fluid. The mucosa of the rectosigmoid, and of the sigmoid, for a distance of 6 cm. proximal to this, was the seat of a completely annular, cauliflower-like, ulcerating tumor. The wall of the sigmoid in this area was diffusely indurated. One-half centimeter proximal to the tumor, on the lateral wall of the sigmoid, there was a perforated diverticulum with a surrounding perisigmoidal abscess. The serosal aspect of the sigmoid and the portion of the genital tract forming the perisigmoidal abscess were markedly discolored and covered with exudate. There were two large duodenal diverticula. There were many diverticula throughout the colon containing inspissated fecal material. The pathologic report of the tumor was adenocarcinoma with lymph node metastases.

SUMMARY

In the ten-year period, 1927–1937, 35 cases of diverticulitis of the colon were admitted to the Surgical Services of the Mount Sinai Hospital. Surgical complications were present in 19 of these cases, and 16 cases were uncomplicated. The complications consisted of peritonitis without perforation in two cases, perforation with abscess in five cases, perforation with peri-

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tonitis in five cases, peridiverticulitis (stenosis) in four cases, sigmoidovesical fistula in two cases, and associated carcinoma in one case.

There was a marked difference in the age groups of the two types of cases as shown in Table II.

TABLE II

Type	0-10 Years	10-20 Years	20-30 Years	30-40 Years	40-50 Years	50-60 Years	60-70 Years	70-80 Years	80-90 Years	Average Years
Uncomplicated cases.....	0	0	0	0	0	2	7	6	1	69
Complicated cases.....	1	0	1	5	3	5	2	2	0	51

A case of diverticulitis of the colon in an 18-hour-old infant was reported, which is the youngest case on record.

The symptoms in the uncomplicated cases were, in the order of frequency, lower abdominal pain, constipation, diarrhea, blood in stools, and vomiting. The symptomatology in the complicated cases was determined by the type of complication present. Positive findings were not always found on physical examination in the uncomplicated cases, but the diagnosis of diverticulitis was confirmed roentgenologically. In the complicated cases, the findings on physical examination were those of the complication present in the individual case. The sigmoid was the most frequent site of disease, but in two cases there was a perforation of a diverticulum of the splenic flexure of the colon.

The uncomplicated cases were not operated upon, and subsided under conservative therapy. The operative mortality in the cases with surgical complications was high—62 per cent. The salient facts in the fatal cases give some of the reasons for this high mortality.

There was one death in the two cases with peritonitis without perforation. This patient had a diffuse peritonitis of eight days' duration. There were three deaths in five cases with perforation and abscess. In the first case, a Mikulicz exteriorization in addition to the drainage of the abscess was performed. A gangrenous inflammation of the abdominal wound and the tissues surrounding the operative site contributed to the fatal issue. The remaining two patients were in poor condition, with large, multilocular abscesses, in whom the drainage of the abscesses did not influence the course of the disease.

There were four deaths in the five cases with perforation and peritonitis. These patients had advanced, diffuse peritonitis. Two of these patients were so toxic that operation was not performed. The third death was that of the 18-hour-old infant. The fourth patient was operated upon within a few hours of admission without adequate preoperative therapy. There were two deaths in the four cases with peridiverticulitis. One patient had an advanced intestinal obstruction. He refused operation, and died the day following admission. The other patient had a primary resection of the sigmoid with an end-to-end anastomosis. There was no autopsy, but there were clinical evidences of peritonitis. The two patients with sigmoidovesical

fistulae died. One patient had a primary resection of the sigmoid with an end-to-end anastomosis. Death was due to leakage of the suture line and peritonitis. The other patient had advanced perisigmoidal suppuration. The patient with associated carcinoma died of a peritonitis secondary to the perforation of the diverticula of the sigmoid.

The cases in this paper were from the surgical services of Drs. Edwin Beer, Albert A. Berg, Ralph Colp, Charles A. Elsberg, Richard Lewisohn, Alexis V. Moschcowitz and Harold Neuhof. The author wishes to express his appreciation to these heads of services for the use of these cases.

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THE PRODUCTION OF HYPER- AND HYPOMOTILITY OF THE MUSCULATURE OF THE SMALL BOWEL IN THE HUMAN

EXPERIMENTAL STUDIES ON THE:

- (A) NORMAL PERISTALTIC ACTIVITY
- (B) EFFECT OF MORPHINE
- (C) EFFECT OF ATROPINE

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ADVANTAGE was taken of a case of intestinal prolapse or bowel exteriorization (involving the lower one-third of the ileum) in an otherwise healthy male to record daily circular and longitudinal muscle activity of the exposed bowel. The loop of exteriorized ileum was 12 inches in length with an artificial anus at its summit so that the lower limb of the loop was constantly empty. The method of recording, described by Alvarez,¹ was adapted in the following manner: Two Wiggers myocardiographs were fastened to four permanent nonabsorbable sutures loosely encircling a mass of circular or longitudinal muscle, as is shown in Fig. 1. The longitudinal fibers selected were on the antimesenteric border of the limb of the loop traversed by intestinal contents. The sutures that encircled these were approximately two and one-half inches apart. The bundle of circular fibers selected crossed these at about their middle and the sutures around these were about one and one-half inches apart. Rubber tubes were used to transmit variations in pressure from the receiving myograph to a recording tambour of the fall away lever type. A watch timer was used to record time in six-second intervals, and also to serve as a base line. The apparatus was so arranged that it could be set up in working order at the bedside of the patient without changing his position and might be used with the patient in either a lying or semisitting position.

Continuous kymographic tracings were thus taken daily from the same segment of exposed lower ileum before, during, and after the administration of pharmacopoeal and clinical doses of a drug. The "normal" peristaltic activity during the preinjection period served as a satisfactory basis for comparison of pharmacodynamic effects on intestinal muscle.

The effects recorded were also visually observed with regard to expulsion of intestinal contents from the visible anus and could be correlated with propulsive and nonpropulsive intestinal movement.

The following general precautions were observed in all experiments: The patient was prepared in no way for the experiment with the exception that any medication he might have been taking was discontinued the night

Submitted for publication July 10, 1939.

MOTILITY OF SMALL INTESTINE

before. All experiments were conducted two hours following meals. To obviate reactions to the mechanical stimulus, tracings were not taken until at least 20 minutes after attachment of the myographs to the sutures in the bowel. The experiment was usually discontinued when the patient began to

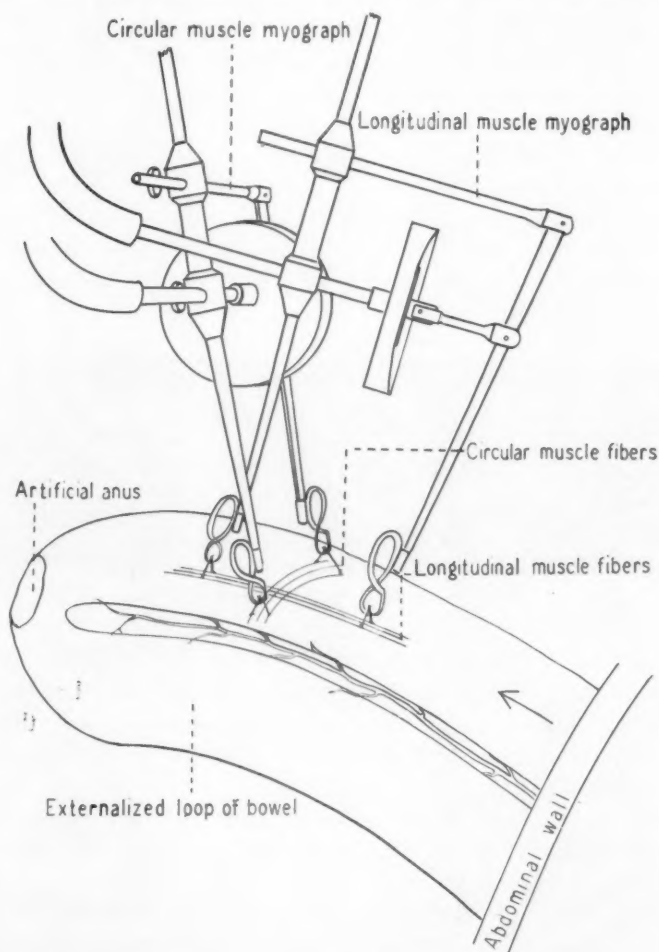


FIG. 1.—Illustrates, schematically, the set-up employed to register the motor activity of the musculature of the small intestine.

complain of pain or fatigue. During the experiment, the exposed bowel was kept covered with saline pledgets and a rubber dam to prevent evaporation. A 75-watt drop light maintained external heat.

RESULTS.—“Normal” Peristaltic Activity: It was noted in a study of the first 20 to 30 minutes of each experiment that there were periods of activity and periods of inactivity, and that during the periods of activity certain contractions were effective in producing a forceful expulsion of intestinal contents. For the period of activity to be most effective in producing propulsion

we noted that both muscle coats worked simultaneously but the onset of longitudinal muscle contraction preceded that of circular muscle contraction by from one to one and one-half minutes and continued after contractions in the circular muscle had ceased. That is to say that the duration of longitudinal muscle contraction was always greater than the period of circular muscle contraction. We, therefore, refer to this series of synchronous contractions as the "peristaltic" wave. Two such peristaltic waves are shown in Graph 1. This wave occurred normally one to six times during a 30-minute preinjection period and had an average duration of from one to six minutes.

All other intestinal activity not effective in causing propulsion we classified as the "mixing" wave. These are single contractions followed by equal phases of relaxation with an average duration of six to 12 seconds each. In our records this wave appeared normally nine to 150 times during a 30-minute period.



GRAPH 1.—Showing "normal" intestinal activity.
Key.—A: Base line and time in six-second intervals.
B: Longitudinal muscle contraction.
C: Circular muscle contraction.

In the records, changes in either circular or longitudinal muscle tone are shown by increase or decrease of either writing line from the base line (Graph 1). An increase in this distance (A-B, or A-C) represents an increase in muscle tone.

Experiments were made with morphine sulphate, atropine sulphate, pilocarpine hydrochloride, pituitrin, pitressin, prostigmin, Hartmann's solution, and 5 per cent glucose.

Effect of Morphine Sulphate.—There are four experiments undertaken to show the effects of the intramuscular injection of morphine sulphate. The morphine was given into the deltoid muscle two hours following a regular hospital meal. The dose was gr. $\frac{1}{8}$, followed in 20 to 30 minutes by gr. $\frac{1}{8}$. In two of the four experiments a third injection of gr. $\frac{1}{8}$ of morphine was given (Table 1).

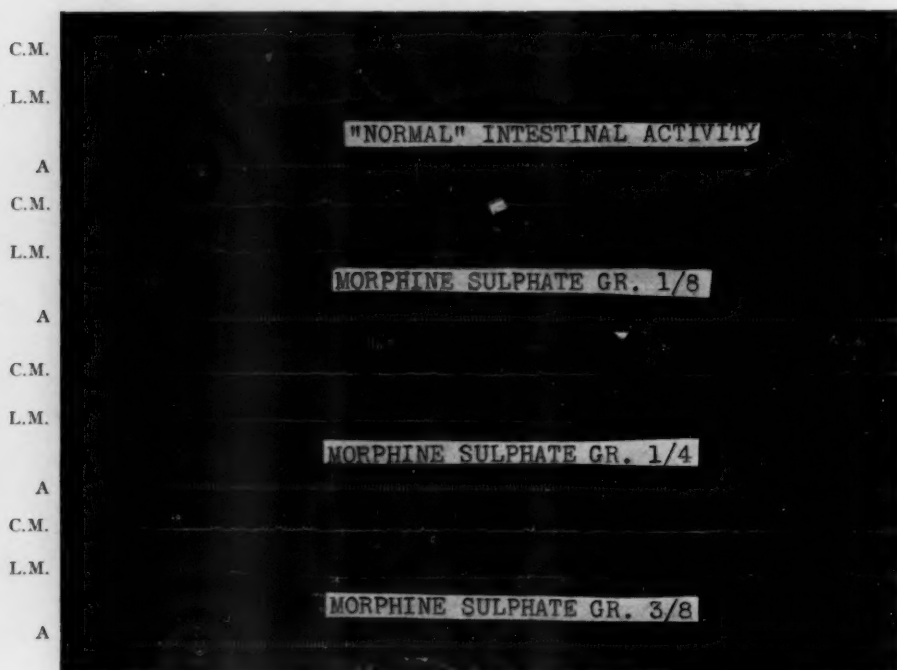
Intestinal activity before and after morphine administration was recorded in Experiment III as shown in Graph 2. In all experiments a complete suppression of propulsive activity followed morphine gr. $\frac{1}{8}$. The frequency of the "mixing" wave was increased in all experiments. The first effects appeared two to four minutes following administration. Circular muscle tone was slightly increased in Experiments I and IV but remained unchanged in

[illegible]

Experiments II and III. Longitudinal muscle tone remained unchanged in the first two experiments but was increased in Experiments III and IV by morphine gr. $\frac{1}{8}$.

In all experiments a second dose of gr. $\frac{1}{8}$ decreased the frequency of the "mixing" wave and increased the muscle tone of both coats.

When a total of three gr. $\frac{1}{8}$ doses of morphine had been given the frequency of the "mixing" wave was increased in Experiment II from 150 to 195, and decreased in Experiment III from 160 to 120.



GRAPH 2.—Showing the effect of the injection of a varying dosage of morphine sulphate (Gr. $\frac{1}{8}$ — $\frac{1}{4}$ — $\frac{3}{8}$) in comparison with the "base line" graph showing the "normal" intestinal activity.

Key.—C.M.: Circular muscle contraction.

L.M.: Longitudinal muscle contraction.

A.: Baseline and time in six-second intervals.

Effect of Atropine Sulphate.—Grain $\frac{1}{150}$ atropine sulphate was given subcutaneously in four experiments and tracings were taken in the manner described, approximately two hours following the midday meal.

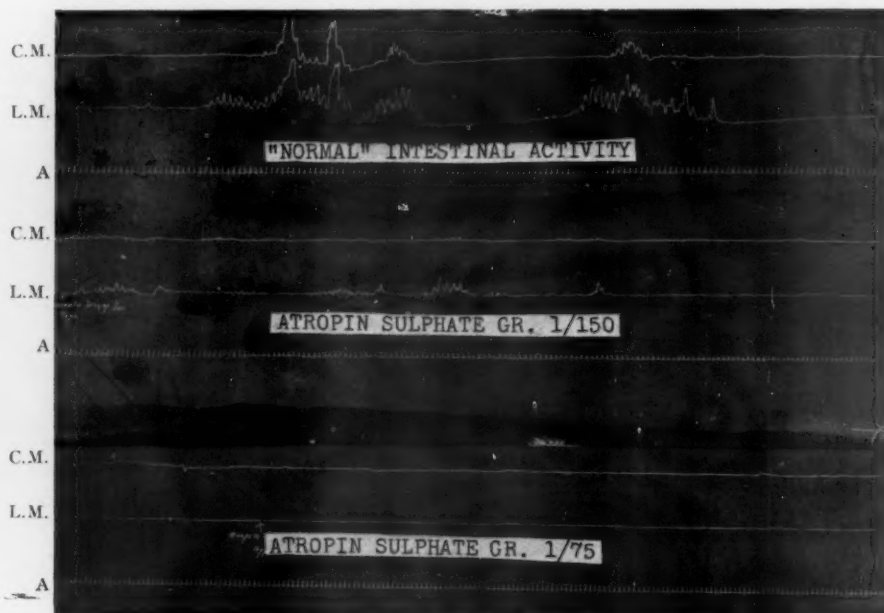
In all four experiments propulsive and nonpropulsive activity was decreased following gr. $\frac{1}{150}$ atropine sulphate. Intestinal activity before and after atropine administration was recorded in Experiment IV as is shown in Graph 3.

In Experiment IV, two peristaltic waves were recorded during the pre-injection period. The atropine was then given, and, from there on, a complete suppression of all propulsive activity ensued (Graph 3). In Experiment I, the frequency of the peristaltic wave was decreased from six to three;

in Experiment II, from five to two; and in Experiment III, from three to zero by gr. 1/150 atropine sulphate.

In all experiments there were no peristaltic waves recorded following the second injection of gr. 1/150 atropine.

In all experiments, circular muscle tone remained unchanged following either the first or second injection of atropine. Loss of longitudinal muscle tone was demonstrated in two experiments to follow the second injection of atropine.



GRAPH 3.—Showing the effect of the injection of a varying dosage of atropine sulphate (Gr. 1/150–1/75) in comparison with the "baseline" graph showing the "normal" intestinal activity.

Key.—C.M.: Circular muscle contraction.

L.M.: Longitudinal muscle contraction.

A.: Baseline and time in six-second intervals.

Discussion.—Whether our observations truly record the action of circular or longitudinal muscle alone, may be questioned. One is well aware that the circular muscle is not strictly circular nor is the longitudinal strictly longitudinal, but rather that their fibers intermingle and deviate more or less from the coronal or sagittal planes of the intestine in which they happen to lie. Such variations, however, may be ignored and the record of their action, as shown here, may be taken to represent that of the circular and longitudinal muscle in the wall of the human, exteriorized small bowel loop.

As regards the relations between the two muscle coats during a peristaltic movement, Van Braam Houckgeest,² in 1872, observed that the advancing ring of constriction in a peristaltic movement was immediately preceded by a shortening of the longitudinal muscle fibers. Bayliss and Starling,³ in 1901, observed that both muscle coats were affected in the contraction above and relaxation below. Krishnan,⁴ in studying the peristaltic action of cats,

in 1932, concluded that: In a peristaltic movement, a wave of longitudinal muscle contraction with relaxation of the circular muscle preceded a wave of circular muscle contraction with relaxation of the corresponding longitudinal muscle by a full wavelength. Our findings in man were the same as those observed by Krishnan in the cat except that we found the interval of time between the onset of contraction of both muscle coats to vary between one-half to one and one-half minutes. Contractions of the longitudinal muscle were also found to continue after activity in the circular muscle had ceased.

According to the law formulated by Bayliss and Starling⁵ in the first of a series of three articles of the movement and innervation of the bowel based mainly on balloon records, "excitation of any part of the gut excites contraction above and inhibition below." Langly and Magnus,⁶ in 1905, and Cannon,⁷ in 1912, point out that this myenteric reflex was not always present and often was hard to demonstrate. Alvarez and Mahoney,⁸ in 1924, report that, in a large number of observations, there was a preliminary rise in tone, which was just the opposite of what the law required. Alvarez and Zimmerman,⁹ in 1927, with the help of the motion picture camera, found that if this widening of the bowel did occur it was due to a distention and not to an inhibition. Krishnan, in 1933, states: "That, because of the contraction of the longitudinal muscle preceding the peristaltic wave, the gut distal to the wave was shortened and dilated." We were unable to demonstrate, as suggested by Krishnan, the dilatation of bowel before the onset of the peristaltic wave because of the preceding longitudinal muscle contraction, nor were we able to show, in any of our records, an inhibition or dilatation of either muscle coat preceding the peristaltic wave.

Our results following the administration of morphine do not entirely coincide with those of previous investigators. Pancoast and Hopkins,¹⁰ in 1915, concluded, from roentgenologic evidence, that no small intestinal effect followed morphine. In 1926, Plant and Miller¹¹ found that the number of contractions of small bowel seen through a thin-walled hernial sac in man were increased by morphine. Dvorack, *et al.*,¹² and Orr and Carlson,¹³ both using the balloon technic of recording, report increased peristaltic activity following small doses of morphine (10 mg.). Orr and Carlson further report that large doses of morphine stopped peristaltic activity without altering the frequency of the "mixing" wave. Abbott and Pendergrass,¹⁴ using the intubation tube described by Abbott and Miller, noted that morphine produced, in the upper small bowel, a brief period of stimulation followed by depression, but that frequently the distal coils of ileum did not exhibit any reaction, or merely the phase of depression.

CONCLUSIONS

Activity of the exteriorized lower small bowel in man is either propulsive or nonpropulsive in nature.

The "peristaltic" wave in the lower three feet of the small bowel, effective in producing a propulsion of intestinal contents, occurs one to six times

during 30 minutes, with an average duration of from one to six minutes each. This wave consists of a simultaneous contraction of both muscle coats with the onset of longitudinal muscle contraction preceding that of the circular muscle from one to one and one-half minutes and continuing after contractions of the circular muscle have ceased.

The "mixing" wave is ineffective in causing a propulsion of intestinal contents and consists of single contractions followed by equal phases of relaxation. These waves occur nine to 150 times during 30 minutes with an average duration of from six to 12 seconds each.

Morphine sulphate in gr. $\frac{1}{8}$ doses completely suppresses the "peristaltic" wave, but increases the frequency of the "mixing" wave. A second injection of gr. $\frac{1}{8}$ morphine, 20 to 30 minutes later, decreases the frequency of the "mixing" wave and increases the tone of both muscle coats.

Grain $\frac{1}{150}$ atropine sulphate decreases the frequency of both peristaltic and "mixing" waves. A second injection of atropine, given 20 to 30 minutes later, produces a complete suppression of the "peristaltic" wave, an almost complete absence of the "mixing" wave, and an occasional loss in tone of the longitudinal muscle coat.

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ADENOMA OF THE ISLETS OF LANGERHANS, WITH HYPER-INSULINISM, ASSOCIATED WITH ADENOMA OF THE THYROID

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COWLEY,⁶ in 1788, first suggested that the pancreas was disordered in diabetes. In 1869, Langerhans¹⁹ discovered the islet cells in the pancreas, but it was not until 1900 that Ssobolew²³ and Schulze²¹ independently discovered their physiologic significance. Banting³ and his coworkers, in 1922, discovered insulin and shortly after that Seale Harris¹¹ coined the word "hyperinsulinism" and used it to apply to patients in whom there was an abnormally low blood sugar associated with certain symptoms of a more or less definite type, such as one sees from administering too much insulin to diabetics.

The first case of hyperinsulinism due to an islet cell tumor was reported in 1927 by Wilder and W. J. Mayo.²⁸ This patient was a physician who had a malignant tumor of the islet cells. He was operated upon and eventually died. Biologic assays of the tumor tissue removed definitely proved its insulin activity and correlated perfectly with the clinical phenomena. Roscoe Graham¹³ of Toronto, in 1929, reported the first case of hyperinsulinism cured by surgical removal of an islet cell tumor. Since this original case report, there has been an increasing number of patients operated upon for suspected tumors of the islet cells. Allen O. Whipple²⁴ in all probability has operated upon more cases than any other surgeon. Up until a few months ago, he had operated upon 14 cases with two deaths. In every case but one he found one or more adenomata to be present.

The case which is being reported herewith is of unusual interest because the patient is one of the oldest reported having this disorder, and because an adenoma of the thyroid complicated the picture.

Case Report.—Hosp. No. 35—1436: M. V., white female, age 56, was admitted to the St. Francis Hospital, November 16, 1935, and referred to the Neurologic Service of Dr. J. G. Lloyd on account of episodes of unconsciousness of two and one-half years' duration. The first attack came on while she was in the theater and resembled a fainting seizure. Subsequent to this she suffered from attacks at irregular intervals, usually every seven to ten days at the onset, but becoming progressively more frequent and more severe so that at the time of admission they occurred two to three times a week, and lasted as long as 17 hours. The attacks were most likely to come on in the morning before breakfast. To avert these attacks the patient's daughter had learned to set the alarm at 3 A.M. and feed her mother.

The mild attacks appeared as simple fainting spells from which the patient recovered rapidly, whereas the severer spells found the patient in deep unconsciousness

Submitted for publication May 26, 1939.

HYPERINSULINISM

from which she could not be aroused by shaking. At times there was jerking of her extremities during the attack, but for the most part she was limp and relaxed and had involuntary urination and defecation with profuse perspiration. Before becoming unconscious the patient would seem to lose the power of speech and develop a stare, although she was perfectly aware of events preceding her unconsciousness. After an attack the patient usually felt weak and thirsty.

Between attacks the patient appeared perfectly normal at times, but the family did notice a tendency to a personality change; that is, whereas before the patient began suffering from the attacks she was of a cheerful cooperative disposition, as the disorder progressed she showed a tendency to become uncooperative and cantankerous.

The patient knew she had had a goiter for 20 years. About five years prior to admission to the hospital she thought she weighed between 120 and 130 pounds, and she had been losing weight since then. In addition to loss of weight, she complained of heat intolerance, rapid heart action, nervousness and tremor of the hands. The diet of the patient had been restricted during the last two years, particularly as regards meat and carbohydrates.

The rest of the history was irrelevant save for a record several years previously of an attack of severe abdominal pain associated with jaundice. The family physician said she had liver trouble at that time.

Physical Examination.—The patient was markedly emaciated, weighing about 80 pounds. Color was fairly good. The patient was edentulous. The thyroid gland was enlarged, particularly in the region of the isthmus and left lobe, where there was a definite adenoma, approximately 4 to 5 cm. in diameter. The patient had a scoliosis of the upper thoracic vertebrae to the right. Heart rate was rapid. Systolic murmurs were present over all valve areas, transmitted to the axilla; A₂ was greater than P₂. Blood pressure 160/90. No bruit was noted over the thyroid gland. Skin was warm, not particularly moist. A fine tremor of the fingers was present. No abdominal masses were palpable. Pelvic examination showed evidence of atrophic changes in the cervix and vagina. Uterus could not be definitely outlined. Rectal examination was negative. There was moderate quadriceps weakness, but no edema of the legs. Eyegrounds essentially normal.

Laboratory Data.—Many laboratory procedures were carried out, the most significant of which were the low blood sugar and high basal metabolic rates. The blood sugar taken November 18, 1935, was so low that it could not be read. A recheck of the blood sugar the following day showed the reading to be 34 mg. A basal metabolic rate taken November 19, 1935, was +54 and a recheck the following day was +65. Urinalysis showed a normal specific gravity and a faint trace of albumin with a few casts and pus cells. Blood count showed hemoglobin of 70 per cent, R.B.C. 3,400,000, W.B.C. 7,300 and an essentially normal differential count. Blood Wassermann and Kahn were negative. Blood chemistry: Calcium 10.9 mg.; magnesium 2.9 mg.; N.P.N. 28.8 mg.; creatinine 1.58 mg.

Roentgenologic examination of the skull was normal. The chest showed evidence of an inactive bilateral tuberculous process. A lateral view showed no evidence of a mediastinal tumor.

It was assumed that the patient had a toxic, adenomatous goiter and hypoglycemia based on the clinical and laboratory data. It was decided to operate upon the thyroid gland first, and she was prepared accordingly, using a high caloric diet with plenty of carbohydrate and Lugol's solution preoperatively. On this regimen the patient seemed to improve and the spells of unconsciousness became less frequent. Nine days after admission to the hospital, she experienced an attack of unconsciousness, and a blood sugar taken at that time was 32 mg. The patient promptly responded to 10 per cent glucose given intravenously. Blood sugars taken on December 2 and December 9, 1935, were reported as nil and 57 mg. respectively. Basal metabolic rates taken on December 2, 5 and 9, 1935, were reported as being +35, +24, and +12 per cent (Chart 1).

The patient's goiter was operated upon December 12, 1935, and a left lobectomy

performed, excising an adenoma about 4 x 5 cm. in diameter. The pathologic report, Path. No. S-2969-35, was cystic adenoma of the thyroid and hyperplasia of thyroid (exophthalmic type).

Subsequent Course.—During the course of the operation and for 24 hours postoperatively, 10 per cent glucose in normal saline was administered continuously intravenously. Following this, intravenous glucose was given intermittently postoperatively for an additional 24 hours. The patient made quite a satisfactory convalescence save for one spell of coma about one week postoperatively. At this time her blood sugar was 35 mg. By feeding her coffee and sugar, she quickly responded. She was discharged from the hospital, December 21, 1935, with advice regarding an adequate intake of food, particularly carbohydrates.

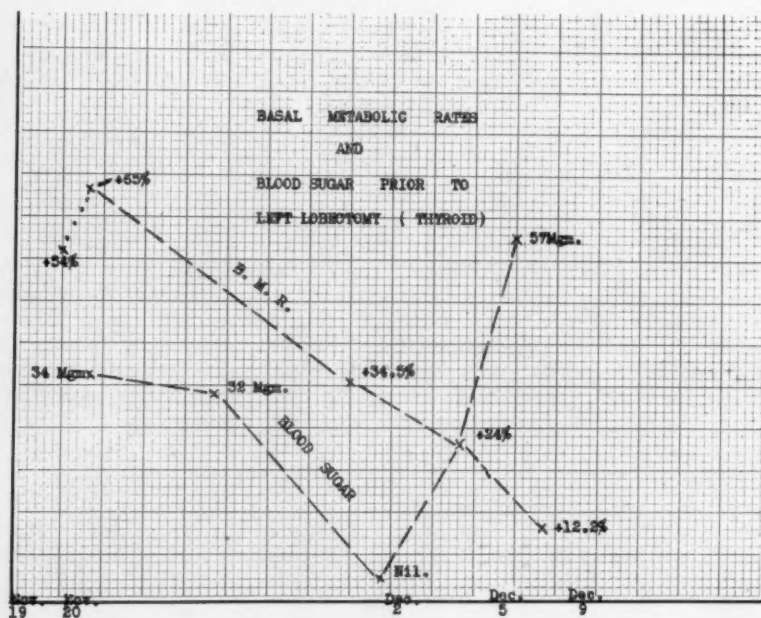


CHART I.

She was observed over a period of about a year and showed a marked improvement in her general health with a gain of 30 pounds in weight, and a marked diminution in the number and severity of attacks attributable to the low blood sugar. In over a year she had had only two episodes of complete unconsciousness, but had had several seizures which were averted by the timely administration of sugar.

March 5, 1936: blood sugar 59 mg.; basal metabolic rate 22. A sugar tolerance test and basal metabolic rate were determined synchronously, March 7, 1936, with the following results:

Sugar Tolerance Test

57 mg. Before ingestion of 80 Gm. glucose
218 mg. 45 min. after ingestion of 80 Gm. glucose
280 mg. 2 hrs. after ingestion of 80 Gm. glucose

Basal Metabolic Rates: +23 Before ingestion of glucose
+22.5 Taken 1 hr. after ingestion of glucose

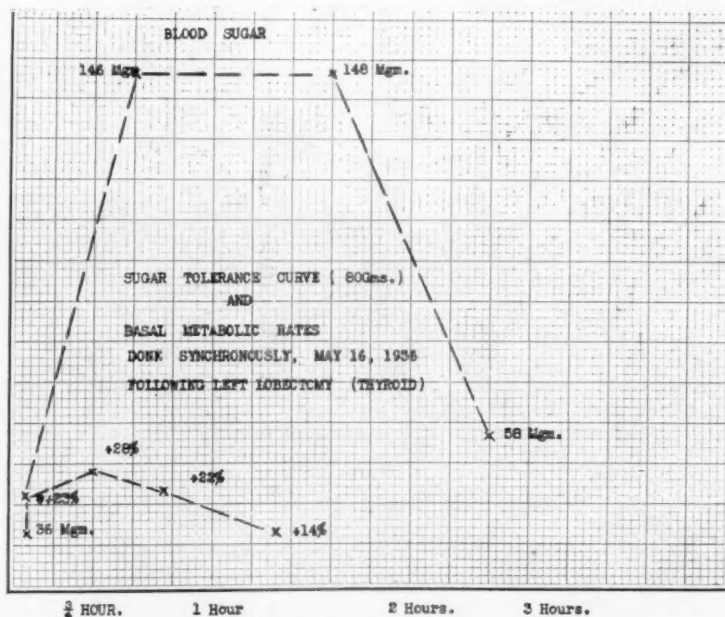
May 16, 1936, she had the same procedure carried out with the following results:

HYPERINSULINISM

Sugar Tolerance Test

Blood Sugar: 36 mg. Before ingestion of 80 Gm. glucose
146 mg. 45 min. after ingestion of 80 Gm. glucose
148 mg. 2 hrs. after ingestion of 80 Gm. glucose
58 mg. 3 hrs. after ingestion of 80 Gm. glucose

Basal Metabolic Rates: +22.8 Before ingestion of 80 Gm. glucose
+27.4 $\frac{1}{2}$ hr. after ingestion of 80 Gm. glucose
+22.5 1 hr. following the above
+14.2 $\frac{3}{4}$ hr. following the above (Chart 2)



August 20, 1936: Blood sugar 35 mg. In view of the incomplete relief of the symptoms, the patient was readmitted to the hospital, Hosp. No. 55582, January 27, 1937, for exploration of the pancreas. Diagnosis: Adenoma of islets of Langerhans.

January 28, 1937: Blood sugar 25 mg.; basal metabolic rate —1. On February 1, 1937, the pancreas was explored, giving full glass of orange juice and one ounce of sugar three hours preoperatively to the patient. The operative note follows:

Operation.—Dr. D. P. Greenlee: Under ethylene-ether anesthesia, a high left rectus incision was made. The pancreas was explored by opening through the gastrocolic omentum. A tumor about 1½ cm. in diameter was found situated in the body of the pancreas near its junction with the tail lying close to the inferior border. This was removed by placing clamps on either side of the tumor and removing a wedge shaped piece of pancreas. Bleeding was controlled by using a running mattress suture. The splenic vein was visualized at the posterior, upper border of the pancreas. A cigarette drain was introduced down where the tumor had been removed from the pancreas. The rent in the gastrocolic omentum was sutured. The gallbladder contained at least one gallstone, and there was moderate associated hepatitis. Exploration of the rest of the upper abdomen was negative and the remainder of the pancreas was explored and no

further tumors found. At the start of operation a continuous venoclysis of 10 per cent glucose in normal saline was started, and this was used throughout operation.

Pathologic Examination.—*Gross:* Path. No. S-221-37, Dr. A. J. Bruecken. The specimen consisted of a tumor and pancreatic tissue from the inferior portion of the pancreas, and measured 2.8 x 2.0 x 1.8 cm. over all. The surface had a thin connective tis-

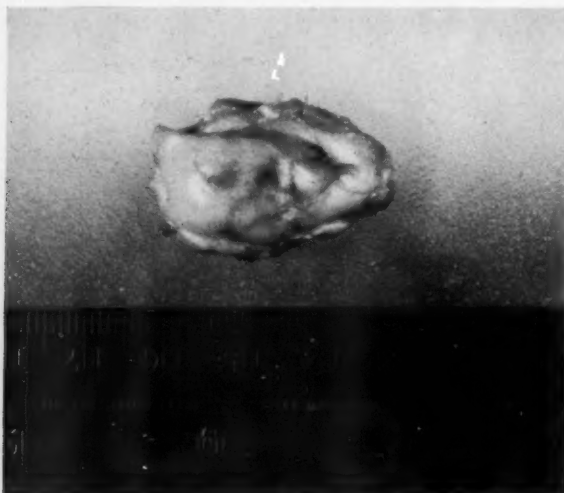


FIG. 1.—Gross appearance of specimen.



FIG. 2.—Cut section of tumor.

sue covering, slightly blood stained. Beneath this, the tissue had a light, brownish-yellow, lobulated appearance. Three-fourths of the circumference of the specimen had a ragged edge while the remainder had a smooth, regular margin. On palpation, there was a central round area of quite firm consistency, surrounded by soft, meaty pancreatic tissue; this central firm area was not visible on the surface, being completely enclosed by pan-

creatic tissue. On section, there was found to be a firm, yellowish-gray, somewhat fibrous and faintly granular appearing, definitely encapsulated, rounded tumor mass which measured $1.7 \times 1.5 \times 1.2$ cm. The cut-surface was smooth and greasy. At one side of the tumor there was a small area showing several pinpoint-sized, red areas resembling hemorrhage within the tumor. Surrounding the tumor was brownish-yellow pancreatic tissue showing the usual glandular appearance. The greater portion of the tumor lay 2 Mm. beneath the surface of the pancreas; this 2 Mm. was composed of pancreatic tissue with its external, thin fibrous membrane. The entire specimen weighed 3.5 Gms. The tumor was intact and could be easily shelled out of its capsule (Figs. 1 and 2).

Microscopic: Section of the mass with surrounding pancreatic tissue showed the latter and a marked dilation of the large duct in it. The mass showed

a definite capsule of fibrous tissue separating it from the surrounding pancreatic tissue for only a part of its extent. In the other part, while the lobules of the growth were each surrounded by a fibrous capsule and distinct, nevertheless they were located directly within the acinar lobules of the pancreatic tissue, and furthermore a few isolated acini

of the latter extended into the growth for a short distance. The growth was composed of irregular masses of cells which varied greatly in size and in the amount of surrounding connective tissue. The largest mass bore some resemblance to a markedly hyperplastic thyroid nodule and there was marked retraction of the stroma processes with a very abundant blood supply and no evidence of necrosis. The rounded portions of the growth distinctly recalled islets of Langerhans, but some of the larger formations suggested a papillary, adenomatous structure, and in fact one could easily demonstrate a glandular tubule and rarely some inspissated secretion in such a tubule. The cells were sometimes arranged in a continuous mass or column without stroma partitions which produced a pseudoglandular appearance elsewhere. The

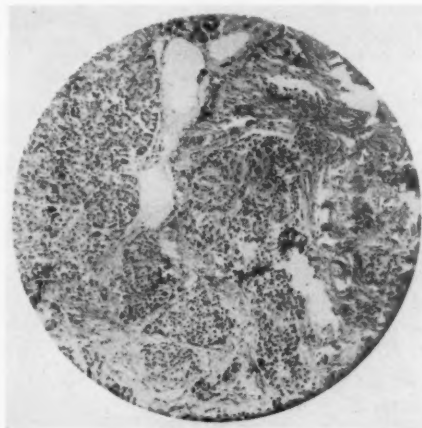


FIG. 4.—Low power—showing relation of tumor to acinar pancreatic tissue in upper left. Islands of tumor cells in lower portion, with increase of vascular stroma on the right.

cells appeared fairly uniform but there were some distinct variations. With the present H. & E. stain they appeared compact, polygonic, medium-sized with round or oval nuclei showing small nucleoli and in general not unlike greatly enlarged dense islet cells or simple columnar epithelium of the ducts. The adjacent islets showed much smaller cells. There was also a distinct tendency in places to form a regular basal row of cells like lining epithelium. Under the capsule-like structure between the adherent pancreatic tissue and the growth there was a very marked replacement of the tumor cells by fibrous tissue. This recalled receding mammary lobules. There was, therefore, a distinct intermingling

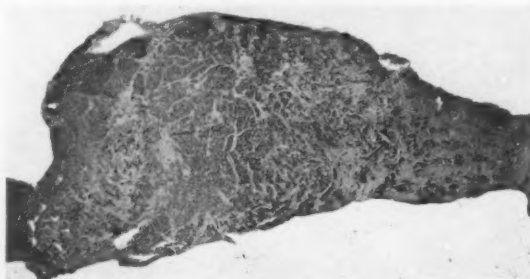


FIG. 3.—Very low power—showing surrounding pancreatic tissue on the left and scirrhus type of growth on the right.

between the growth and surrounding pancreatic tissue but only at the margins. No-where else could one find pancreatic tissue within the confines of the growth. The large amount of collagenous stroma in the growth was noteworthy. Further study revealed a considerable number of structures resembling ducts with quite tall epithelial cells. There were a considerable number of cells with large, and sometimes irregular, nuclei and with prominent nucleoli which were basophilic, and rarely a definite mitotic figure was encountered. Inflammatory cell infiltration was entirely absent save for a very few lymphocytes at one or two points in the stroma.

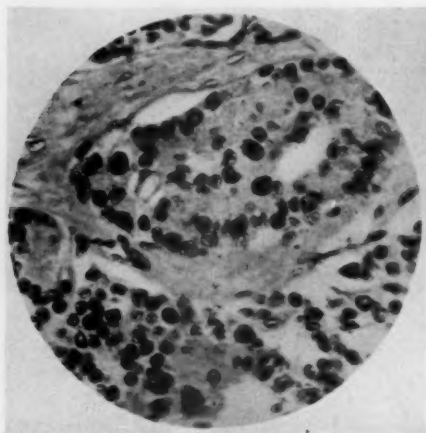


FIG. 5.—High power—showing resemblance to islet tissue and intimate relation to capillary blood vessels lined more or less by tumor cells. Pronounced polymorphism and mitosis of cells.

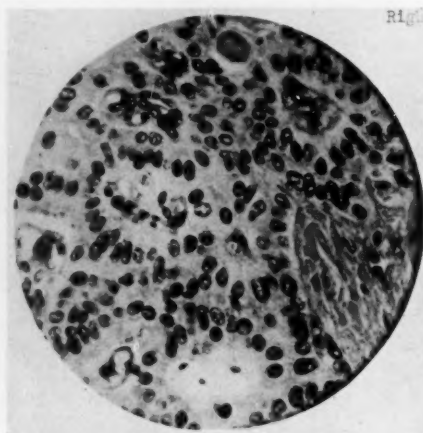


FIG. 6.—Tubular formations, intimate relation to capillaries, more uniformity and inspissated secretion in tubule in uppermost portion.

Another section showed a still more scirrhus picture, with a heavy stroma equaling the glandular tumor tissue. Rarely a giant cell with several large deeply staining nuclei was seen above or within a cell mass. The cells of the growth appeared larger than any of the surrounding pancreatic tissue, namely, acinar, islet and duct cells. They may have represented overgrowth of the small connecting tubes of the organ.

E. & M. stain brought out the variations in the characters of cells of the growth more conspicuously and this, together with the irregularity of the masses and the great amount of stroma, suggested unrestricted aberrant growth.

Sections stained by Goodpasture's granular stain after Orth's fixation showed what appeared to be poorly staining mitochondria, and comparing the staining affinity with the surrounding pancreatic islets the tumor cells most nearly resembled *beta* cells taking more blue than red color but showing no definite granules which, however, was not shown in the surrounding islands (Figs. 3, 4, 5 and 6).

Biologic assays of the tumor tissue were made by Dr. W. S. McEllroy, with the following results:

Total weight of tumor tissue..... 0.95 Gm.

Total volume of extract from 0.95 Gm. = 10 cc.

Vol. extract injected = 5 cc. = 0.475 Gm. tissue..

Rabbit Injected

(Starved 36 hrs.)

Time

11:40 A.M.

Blood sugar: 0.083 mg.

11:45 A.M.

Injected 5 cc. of extract

1:07 P.M.

Blood sugar: Nil

Rabbit in shock with convulsions

{ Method of Scott and Best
used in extraction
Control

(Starved 36 hrs.)

Blood sugar: 0.106 mg.

Blood sugar: 0.132 mg.

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1:15 P.M.	Injected 5 cc. 10% dextrose intramuscularly	
1:30 P.M.	Rabbit able to partially sit up	
1:42 P.M.	Blood sugar: Nil	Blood sugar: 0.115 mg.
1:45 P.M.	5 cc. glucose 10% intravenously	
2:27 P.M.	Blood sugar: Nil	

Rabbit injected showed fall in blood sugar with shock and convulsions which were relieved by glucose. Rabbit after intravenous glucose showed rapid improvement and by the next morning behavior was normal.

The reaction induced by injection of material from 0.475 Gm. of tissue believed to be a typical insulin effect.

The patient made an uneventful convalescence from operation save for moderate ileus for a few days postoperatively. The drain was removed on the sixth postoperative day. There was some serous drainage from the wound for about 11 to 12 days following removal of the cigarette drain, but at no time did it produce skin irritation, and chemical study failed to reveal pancreatic enzymes. Blood sugar determinations were made on the third and seventeen days post operatively and were found to 179 mg. and 94 mg. respectively. A blood sugar determination made about five weeks after operation was 95 mg.

Since operation the patient has been completely relieved of her symptoms, and a sugar tolerance test, performed May 13, 1937, showed:

101 mg.	before ingestion of glucose
202 mg.	45 min. after ingestion of 100 Gm. glucose
210 mg.	2 hrs. after ingestion of 100 Gm. glucose
148 mg.	3 hrs. after ingestion of glucose
86 mg.	4 hrs. after ingestion of glucose (Chart 3)

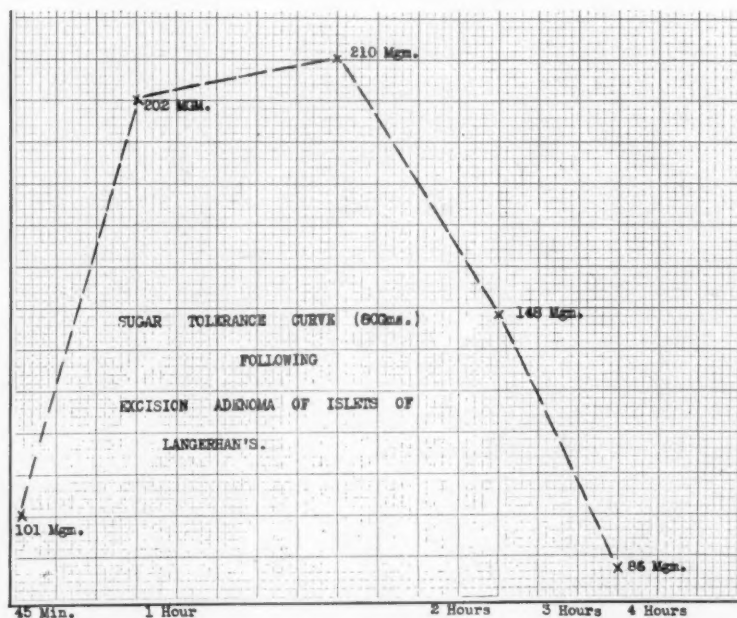


CHART 3.

February 6, 1938: Blood sugar 105 mg.; basal metabolic rate, March 26, 1938,—4. The last blood sugar, determined April 15, 1939, was 90 mg.

Relationship of Thyroid to Hypoglycemia.—In the approach to the management of this case, it was thought that the episodes of unconsciousness were undoubtedly of hypoglycemic origin. In addition to this the patient appeared to be definitely hyperthyroid both from a clinical and a laboratory standpoint.

In hypoglycemia there is a tendency to an increase in basal metabolic rate. This is thought to be an effort to mobilize liver glycogen and combat the tissue glyopenia. Usually, in hyperthyroid states, then, the tendency has been to a hyperglycemic or diabetic state; in low basal metabolic rate states, such as myxedema, there has been a tendency to hypoglycemia.

The findings in this patient, then, were confusing. With advancing years there is a tendency to hyperactivity in an adenomatous goiter—it being estimated by some observers²² that fully one-quarter to one-third of them become hyperactive later in life. There was nothing to prove or disprove that the thyroid disturbance was secondary to the hypoglycemia. It was felt that operation upon the thyroid was first indicated: (1) Because any tendency to a hypoglycemic reaction following the thyroid operation could readily be controlled by administration of intravenous glucose; whereas if the pancreas were first operated upon, there would be much greater difficulty in controlling a hyperthyroid reaction should such occur. (2) It was thought there was some possibility that the patient's extreme emaciation, presumably due to hyperthyroidism, might have so lowered tissue glycogen that a hypoglycemic state resulted. This has been seen¹⁸ on rare occasions in hyperthyroidism.

There was no method of determining whether the patient's hyperthyroidism was independent of the hypoglycemia or whether it was purely a secondary manifestation. If it was a secondary manifestation of the hypoglycemic state, needless to say surgery upon the thyroid was not indicated. Womach and Cole²⁰ have reported a case having signs of exophthalmic goiter with a tendency to hypoglycemia. They first operated upon the pancreas and, although they found no discrete tumor, they did a partial resection of the pancreas with relief of symptoms of hyperthyroidism. They do not advise this procedure in all cases of exophthalmic goiter.

Aitkin² reported a patient having findings typical of exophthalmic goiter; this patient had a thyroidectomy performed. Later, on account of persistency of seizures indicative of hypoglycemia, the pancreas was explored and an adenoma of the islets of Langerhans removed. Since then the patient has developed signs of myxedema and has had to be fed thyroid extract.

However, there have been no cases of adenoma of the islets of Langerhans reported in which hyperthyroidism was associated with an adenomatous goiter.

Diagnosis.—No known procedure to definitely prove that a given case of hypoglycemia is due to adenoma of islets of Langerhans has been devised. Whipple²⁵ has established this triad of findings in hypoglycemia as warranting surgical exploration of the pancreas: (1) Definite repeated seizures of a

vasomotor or a psychic disturbance coming on during the fasting period. (2) A blood sugar reading below 50 mg. per 100 cc. (3) Immediate recovery of the seizure with the intake of sugar.

Two tests have been used to help establish the diagnosis: (1) The insulin tolerance test; and (2) response to adrenalin.

In performing the insulin tolerance test five units of insulin are given intravenously after 12 hours of fasting. After two hours there is no tendency for the blood sugar to reach normal if an adenoma of the islets is present. Fraser⁸ used this method to aid in the diagnosis of a case of adenoma of the islets he has recently reported.

John¹⁴ reported the use of insulin in treating three cases of low blood sugar. He administered 20 units t.i.d. p.c. and gave a high fat diet. This differentiates hypoglycemia of functional from hypoglycemia of anatomic origin. If the patient improved with insulin, the low sugar is most likely due to a physiologic disturbance of the islets. The rationale of the treatment is that by giving exogenous insulin the islet cells are put at rest and return ultimately to a normal functional state.

Adrenalin is administered to rule out any disturbance in glycogen reserve. If the blood sugar does not rise after its administration, it would tend to indicate that the hypoglycemic state might be due to lack of liver or tissue glycogen, rather than to a primary disturbance in the pancreas.

Anatomic and Surgical Considerations.—Various types of incisions have been advocated in exploring the pancreas: (1) The high left rectus which is probably the most common one used; (2) the transverse incision recommended by Whipple;²⁷ and (3) the T-incision used by Finney.⁷

An adequate exposure through a good-sized incision is essential. The pancreas has been most commonly exposed through the gastrocolic omentum, but Judd¹ explored the organ through the gastrohepatic omentum. Whipple²⁶ recommends the use of fine silk ligatures in the pancreas. Tumors have been most frequently found in the region of the body or tail. This is probably due to the fact that the islet cells are most numerous here. The relationship of several important large vessels to the posterior surface of the pancreas must be borne in mind in attacking the organ. These vessels are the aorta, vena cava, the splenic vein and artery, the inferior mesenteric vein, the superior mesenteric artery and vein, and the portal vein. In resecting the pancreas in cases where no tumor was found, Holman¹² recommends splenectomy to adequately control bleeding from the pancreas.

The administration of glucose before, during, and after operation would seem to be a safeguard. It should be administered continuously during operation and for a reasonable period postoperatively. Guerry *et al.*¹⁰ have reported a case in which they resected a portion of pancreas and at the conclusion of operation the patient died with a very low blood sugar. They attributed death to "operative insulin crisis." They do not report any post-mortem findings in this case. Only during the first 20 minutes of operation

was 1,000 cc. of 10 per cent glucose administered intravenously in the case they report.

In examining the pancreas for tumors, a very careful search of the whole gland, both by inspection and palpation, should be made. By incising the peritoneum over the inferior border of the organ, it can be turned up and tumors visualized or palpated more readily. After removing one tumor one should investigate to see if other tumors may be present, as both Whipple²⁷ and Graham⁹ have reported cases with multiple tumors—some of these cases have had only one tumor removed at the original operation and secondary operation has been necessary on account of persistence of symptoms, at which time a second tumor has been disclosed.

Ziskind³⁰ has recently reported a case in which no tumor was noted in the pancreas at operation. A resection of pancreas, together with splenectomy, was then carried out, with the surprising discovery of two adenomata in the resected specimen. There has been a remarkable constancy found in the size of the tumors of the islets; as a rule they are small, being about 1.5 cm. in diameter. However, one exceptional case, removed surgically, mentioned by Whipple, weighed 500 Gm.

Pancreatic fistulae have occurred occasionally postoperatively, but have generally been of relatively short duration and produced little difficulty with the wound. Judd¹⁵ mentions one case he had where the fistula persisted for nine months.

General Considerations.—The terms hypoglycemia and hyperinsulinism have been used loosely, and by some individuals they have been used interchangeably. This is a gross error. Hypoglycemia is simply a laboratory finding, and there are many causes of such a condition. In marked cases of hypoglycemia, definite symptoms are produced—which symptoms are dependent on the low blood sugar and are the same regardless of what the etiology may be. Appended is a list of the causes of hypoglycemia as given by Judd and Rynearson:¹⁷

- (1) Hyperinsulinism
 - (A) Endogenous—Pancreas
 - (B) Exogenous—Insulin.
- (2) Lack of opposing secretions—from disease of suprarenals—tumors of pituitary—any myxedema.
- (3) Lack of glycogen from liver or wasting muscles—renal diabetic, lactation, and starvation.
- (4) Interference with regulating center—overactive vagus.

Judd¹⁶ has reported two cases, explored for pancreatic islet tumor, in which marked liver damage was found, but no tumors were found in the pancreas. Briggs and Oerting⁵ have reported two cases of extrapancreatic hypoglycemia: one a case of cancer of the stomach with extreme emaciation and an atrophic liver weighing 800 Gm.; the second case was one of Addison's disease.

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In borderline cases medical management should be carried out for a considerable length of time. Judd¹⁶ emphasized a physiologic disturbance in the islets from vagus effect, resulting in low blood sugars, and advised against resection in such cases. McCaughan and Brown²⁰ reported seven cases where they had resected relatively large portions of pancreas in borderline hypoglycemic states without satisfactory results. (Such a procedure could be likened to gastro-enterostomy for hyperacidity without demonstrable pathology in the stomach or duodenum. Such gastro-enterostomies never gave relief of symptoms and often created a worse state of affairs than already existed.)

Where operation fails to disclose any gross disturbance in the pancreas, further search of the abdomen should be made before resection of the pancreas. Possible sources of islet adenomata, other than in normal pancreas, are in accessory pancreatic rests or in pancreatic tissue in Meckel's diverticulum or dermoid cysts of the ovary of the female.

The sugar tolerance curve following operation in the case herewith resembles a diabetic curve now. It is altogether conceivable that the patient has a pancreatitis with disturbance in her remaining islet tissue and is a mild diabetic. This would fit in well with the fact that both cholelithiasis and hepatitis were found at operation.

SUMMARY AND CONCLUSIONS

(1) A case has been reported in which hyperfunction existed in both an adenomatous goiter and in an adenoma of the islets of Langerhans; these two conditions were corrected by appropriate surgical therapy.

(2) Biologic assays of the tumor tissue removed from the pancreas definitely proved its insulin activity.

(3) The most important clinical feature of hyperinsulinism is that the attacks of coma or unconsciousness come on when the patient has abstained from food for some time or has exercised; the coma-like episodes are relieved spectacularly by administering sugar.

(4) The importance of blood chemistry in states of unconsciousness, coma, or where there is any mental disturbance of questionable origin cannot be overemphasized.

(5) It is important to differentiate hypoglycemia from hyperinsulinism.

(6) The pancreas should be attacked surgically only in those cases where it seems definitely the source of trouble. It should be realized that there are functional hypoglycemic states where operation is definitely contraindicated.

(7) Where an adenoma or adenomata has been found at operation the results have been spectacular; much more so than in cases where no tumor was found and a resection of the pancreas was carried out.

(8) In doubtful cases, surgical intervention directed to the pancreas is justifiable when other causes of hypoglycemia have been ruled out, bearing in mind that undue procrastination may permit an operable malignant lesion of the islets to become inoperable.

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CONGENITAL HEMOLYTIC JAUNDICE

REPORT OF A CASE WITH NORMAL FRAGILITY AND NORMAL RETICULOCYTE
COUNT, CURED BY SPLENECTOMY

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A HEMOLYTIC type of jaundice is only occasionally encountered in a surgical practice. Of these the majority occur as the result of acute blood destruction from infections or toxins. Nevertheless, a knowledge of the conditions which are known as congenital and acquired hemolytic jaundice is essential because of the frequency with which they must be considered in the differential diagnosis of diseases of the liver, gallbladder and spleen.

Minkowski,¹ in 1900, emphasized the hereditary character of the congenital type and gave an accurate description of the clinical features of the disease. Chaufford,² in 1907, demonstrated the increased fragility of the red cells. Naegeli³ first stressed the importance of the increased spherocytosis of the red cells. This finding has been noted and confirmed by other observers⁴ (Vaughan and Goddard, 1934; Hayden, 1934; Hawksley and Baily, 1934; Paxton, 1935; Thompson, 1936). Hayden⁵ is of the opinion that the anemia, jaundice, splenomegaly, reticulocytosis and increased fragility are all secondary to the globular form of the erythrocyte. Hayden found decreased cell diameter and increased volume-thickness in all of 12 cases examined. The mean corpuscular volume was variable. It appears likely that microcytosis is a characteristic feature of the disease. However, due to the increased thickness of the cells, mean corpuscular volume may be increased to above normal.

Thompson,⁶ from the examination of the spleens from 30 cases presenting the clinical symptoms of hemolytic jaundice, came to the conclusion that hemolytic jaundice is a definite clinical and pathologic entity. He further stated that the reticulocytes are markedly increased in all instances, ranging from 15 to 50 per cent. He also stated that the majority of red cells are microcytes and the presence of microcytosis is necessary for the diagnosis. In all of his cases he reported that there was an alteration in the fragility of the red cells, which persisted together with microcytosis after splenectomy. In 1936, Thompson⁷ reported his series of cases, which had increased to 45, and his conclusions were basically the same as in his article which appeared in 1932.⁶

Medical teaching and writing have led clinicians to expect to find an increase in the fragility of the red cells and an increased number of reticulocytes in the circulating blood in cases of congenital or acquired hemolytic jaundice.

Submitted for publication June 9, 1939.

Chaufford,² in 1907, was the first to recognize an increase of the reticulocytes in the circulating blood as a feature of chronic congenital and acquired hemolytic jaundice. Reticulocyte counts of over 20 per cent have been reported by many authors. Vaughan⁹ reports 35 cases in which reticulocyte counts were made. It was increased in 32 cases, the maximum count being 60 per cent. The count was normal in three cases. No correlation was found between the reticulocytosis and the degree of the anemia.

Gänsslen¹⁰ states that 10 per cent of the cases do not show the typical abnormality of increased fragility of the red cells. Bockus and Tumen¹¹ state that microcytosis and increased fragility are the most constant features of the disease, but that the fragility is normal in about 10 per cent of the cases. They point out that in no other disease is such a high percentage of reticulocytes present.

Baty¹² reports a case in which 92 per cent of the red cells were found to contain reticular material and occasional cells with nuclei and nuclear bodies were seen. Two years after the removal of the spleen the patient showed reticulocyte counts of 30-70 per cent and signs of continued activity of the disease. Reynolds¹³ reports a case of acquired hemolytic jaundice in a 21-year-old male, who was well until 17 months before admission, in whom the fragility of the red cells was only slightly altered and reticular material was present in 95 per cent of the red cells. This patient was cured by splenectomy, and the fragility test over three years following splenectomy was normal.

Some investigators believe that immature red blood cells, at least in certain disorders of the blood, are more resistant to hemolysis by hypotonic sodium chloride solution than are the adult cells, while others hold that this is not the case.

There are in the literature cases of unquestionable chronic congenital or acquired hemolytic jaundice with normal fragility tests and normal reticulocyte counts which were cured by splenectomy. Such a case is presented herewith, because of its several features which are at variance with the usual case of chronic, congenital hemolytic jaundice and because of its very rapid and dramatic cure following splenectomy.

Case Report.—Hosp. No. 31,481: H. M., white, male, age 33, was admitted to the Ball Memorial Hospital, September 11, 1934, complaining of vomiting, weakness, jaundice, pain in the right upper quadrant, and loss of weight.

Onset and Course.—The patient stated that he had been yellow, *i.e.*, jaundiced, off and on all his life. His condition was noticed three days after he was born and had continued to be present ever since. However, there were times when the jaundice was mild and other times when it was quite deep. It did not seem to interfere with his health in any great degree; he was able to work and to carry on a fairly normal life until the onset of his present complaints, which developed on month ago. At that time he had a very severe headache which was relieved after three days, and patient thinks that the jaundice probably deepened at this time. After the headaches were relieved, the patient started to vomit and he was unable to keep food on his stomach for ten days but vomited water only twice during that period. During this time he had pains in his abdomen (R.U.Q.) off and on. The pains would start in the right flank and radiate medially along the line of the lower right ribs to the midepigastria region. One

attack of this pain was definitely colicky in nature, very severe and he vomited considerably. Afterwards he was somewhat relieved. The bad attack occurred about 11 days previous to admission, since which episode he has been improving; he has not vomited since, has had a fairly good appetite, has had but a small amount of pain in the right upper quadrant and, in general, has felt pretty well except for weakness. At present, he is jaundiced but not having any pain, is not nauseated, and tolerates food.

He had lost about 30 pounds during the last month. Varying degrees of jaundice had been present since birth but he had not had itching of the skin. Headaches were rare. Severe one at onset of present illness. Tinnitus and dizziness only when attempting to get up since beginning of present trouble. There had been no cough or hemoptysis. Some dyspnea on exertion. Says he has had heart trouble since 1918 following an attack of "flu." Occasionally ankles swell. No precordial pains. His appetite had been good until onset of present complaint and for the last ten days. Had no trouble in eating fatty foods before onset of complaint. Dyspepsia is caused by cucumbers and unripe bananas. Did not have clay-colored stools during present trouble and there is no history of them having been noticed previously. Has not been constipated. There has been no burning or frequency of urination. Urine is usually fairly yellow, but the color has varied from time to time. No hematuria. Seems to think he passes a normal amount of urine.

The patient does not know about childhood diseases except he recalls having had the mumps. No scarlet fever, no typhoid fever, no pneumonia. Has enjoyed fairly good health.

Family History.—Father, age 58, living and well. Has never been jaundiced. His parents were never jaundiced. Mother died at age of 40, and was never jaundiced. Her parents were never jaundiced. Two brothers living and well. Two sisters and one brother died in infancy. Patient does not know the cause of their death.

Physical Examination.—The patient is a well nourished and well developed white male with a marked icteric tint to skin and sclerae. Is not in pain but appears to be moderately chronically ill. T. 99° F., P. 90, R. 20, B.P. 128/35. No falling of hair; no gross abnormalities of the head. The eyes react to light and accommodations, and their movements are normal. The tongue is somewhat dry; cryptic tonsils; no pharyngeal infection. The thyroid is smooth and small; no cervical adenopathy. The chest shows equal expansion. The lung resonance seems slightly impaired posteriorly; normal vesicular breath sounds, no râles. The apex impulse of the heart is visible in sixth left interspace in midclavicular line, no thrills palpable. Slight enlargement to left. None to right. Right border at parasternal line, left at anterior axillary line, 10 cm. to left of midsternal line. A systolic murmur is heard at the apex and a faint diastolic at the base over the aortic area. Corrigan pulse. B.P. 128/35. Pistol shot femorals. Positive Duroziez's sign. The abdomen is not distended; the spleen is easily palpable and is enlarged inferiorly to the level of the umbilicus and mesially to the left paramedian line. The splenic notch is palpable. There is a definite area of tenderness in the right midclavicular line at the costal margin. No rigidity. The extremities are negative. *Clinical impressions:* Cholecystitis with cholelithiasis. Old inactive rheumatic heart disease with mitral and aortic regurgitation, possible functional component. Chronic, congenital hemolytic jaundice.

Laboratory Data.—Blood, September 11, 1934: Hemoglobin 4.6 Gm., 27.6 per cent, erythrocytes 970,000; poikilocytosis +++; polychromatophilia, +; color index 1.4; leukocytes 2,800, eosinophils 0, lymphocytes 20 per cent, neutrophils, band 10 per cent, polys 70 per cent. Urine, September 12, 1934: Clear, acidity low, specific gravity 1.009, albumin negative, sugar faint trace, crystals 0, leukocytes 0; erythrocytes, epithelial 1 plus, granular +, motile bacilli +++. Blood, September 12, 1934: Van den Bergh, direct reaction and indirect reaction; bilirubin 6.9 mg. per 100 cc. blood. Icteric index 100;

CONGENITAL HEMOLYTIC JAUNDICE

bromsulphalein liver function test normal. Fragility test: Hemolysis commenced at 0.44 per cent, complete at 0.38 per cent.

Price Jones

Erythrocyte Diameter

3 cells at	3.5 microns
4	4.0
6	4.5
14	5.0
19	5.5
40	6.0
8	6.5
4	7.0
2	7.5

Average cell diameter
6 microns

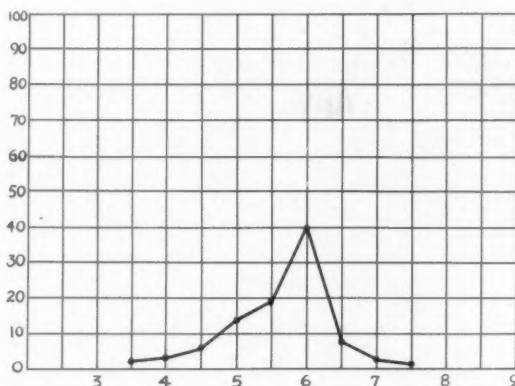


CHART 1.—September 16, 1934:
Showing the diameter of the erythrocytes.

Three days later, September 15, 1934, the patient was given 525 cc. of whole blood by the Kimpton-Brown method with no reaction; this was followed in two days by 700 cc. with no reaction. The following day 675 cc. of blood was given with a subsequent enlargement of the spleen and deepening of the jaundice.

Gastric analysis, September 19, 1934:

Specimens	Fasting	15 min.	30 min.	45 min.	60 min.
Total acidity	2	2	10	6	18
Free acid	none	none	none	none	none
Quantity (cc.)	35	10	8	10	20

No blood found; lactic acid present. Microscopic: Numerous diplostreptococci; many gram-negative and gram-positive bacilli; numerous *Spirochaeta vincenti*; numerous fusiform bacilli.

Blood, September 21, 1934: Hemoglobin 6.4 Gm., erythrocytes 1,760,000, leukocytes 1,900, eosinophils 1, lymphocytes 48, monocytes 3, neutrophils, band 12, polys 36.

The patient was then given 600 cc. of whole blood, September 22, 1934, and 685 cc. whole blood, September 24, 1934. On September 25, 1934, the hemoglobin was 9.4 Gm., 64 per cent, erythrocytes 2,170,000. There occurred increasing signs of blood destruction following the transfusions. One cubic centimeter of concentrated liver extract was administered intramuscularly twice a week. He refused to submit to splenectomy and was discharged, September 29, 1934.

Following discharge, the patient received deep roentgenotherapy to the spleen without benefit, and was readmitted, November 8, 1934, for transfusion, at which time he was given 510 cc. of whole blood, and the following day was given 675 cc. more. The red blood count following these transfusions was 1,910,000, hemoglobin 6.2 Gm., or 37 per cent. He was then discharged but was readmitted, November 20, 1934, at which time he agreed to have splenectomy performed. The red blood count at that time was 1,220,000, hemoglobin 5.4 per cent, and reticulocytes 1.9 per cent. He had approximately 2,200 cc. of whole blood administered during the following week.

Operation.—Splenectomy was performed, December 1, 1934. The spleen was firmly adhered to the diaphragm, but otherwise the operation presented no technical difficulties. The gallbladder was large and full of small stones. It was not removed or opened. He was given 600 cc. of whole blood postoperatively without reaction, and the following day, December 2, 1934, the hemoglobin was 12 Gm., red blood count 3,260,000, reticulocyte

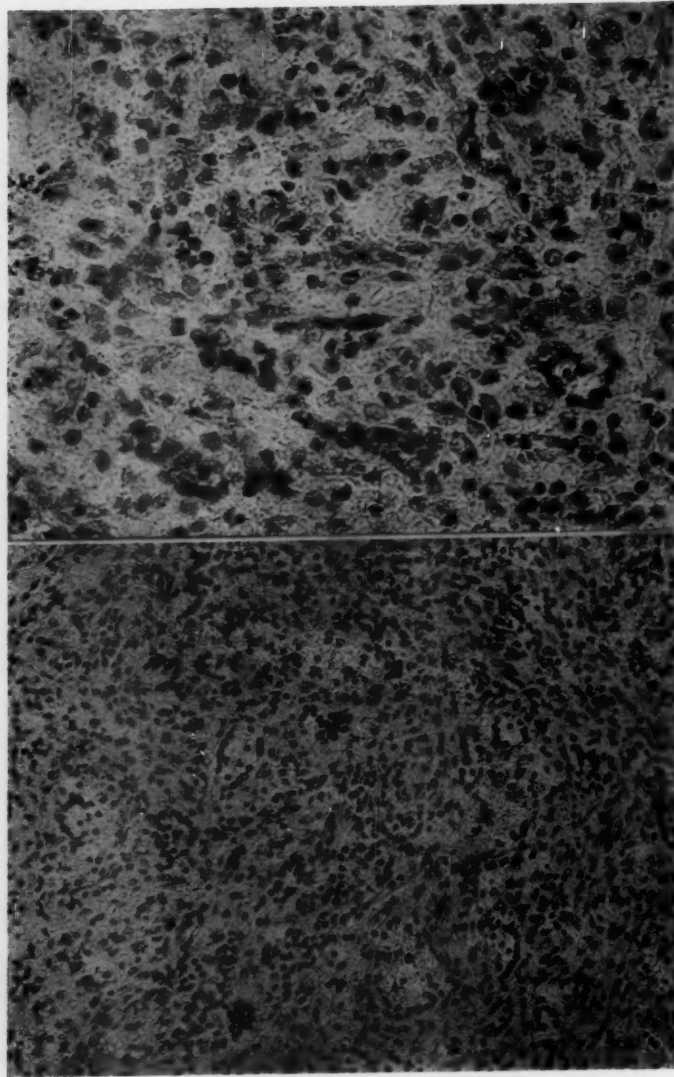


FIG. 1.—A and B: Photomicrographs of the spleen showing striking changes in the splenic sinusoids with the characteristic arrangement of the living cells producing the appearance of pseudo-acini. There is almost complete absence of lymphoid tissue and generalized deposition of pigment. (A: $\times 240$; B: $\times 480$)

CONGENITAL HEMOLYTIC JAUNDICE

count 12.8 per cent, and the leukocytes 20,150, of which 91 per cent were polys. On December 3, 1934, the hemoglobin was 11.8 Gm., red blood count 2,950,000, reticulocytes 11.8 per cent. December 4, 1934, hemoglobin 10.8 Gm., red blood count 2,800,000, reticulocytes 8.4. By this time, which was 48 hours after splenectomy, the jaundice had completely disappeared. Daily blood examinations showed a slow but gradual rise in hemoglobin and red blood count, with a decrease in reticulocyte count to 4.8 per cent on December 12, 1934, and he was discharged in good physical condition, December 19, 1934.

Price Jones	
Erythrocyte Diameter	
2 cells at	3.5 microns
3	4.0
3	4.5
8	5.0
12	5.5
18	6.0
48	6.5
3	7.0
2	7.5
1 cell at	8.0
Average cell diameter	
6.5 microns	

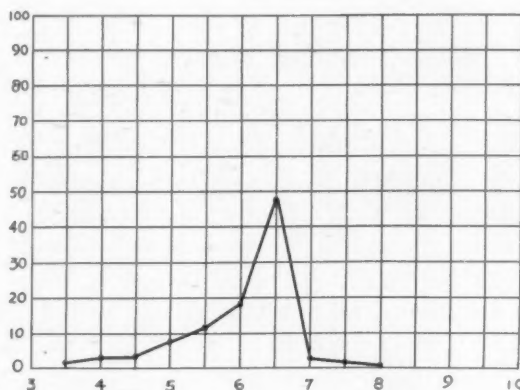


CHART 2.—April 2, 1935: Showing the diameter of the erythrocytes.

Pathologic Examination.—Gross: Dr. Lall G. Montgomery. The spleen weighed 1,577 Gm. and measured 24 x 17 x 6 cm. There is perisplenitis Grade II, especially marked over the diaphragmatic areas, where there is an adhesion to the diaphragm measuring

Price Jones	
Erythrocyte Diameter	
1 cell at	5.0 microns
1	5.5
4 cells at	6.0
8	6.5
82	7.0
2	7.5
2	8.0
Average cell diameter	
7 microns	

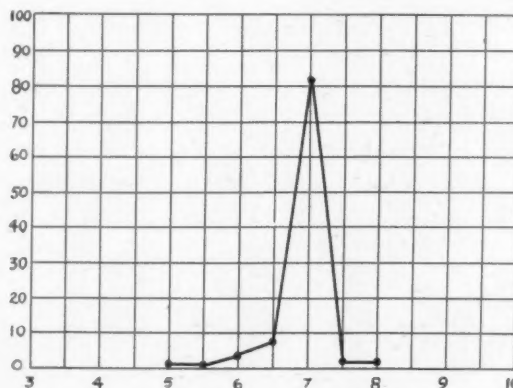


CHART 3.—October 11, 1939: Showing the diameter of the erythrocytes.

5.5 x 3.5 cm. *Microscopically*, the splenic capsule is slightly thickened and there are scattered foci of chronic capsulitis. There are also scattered fibrous adhesions arising from the capsule. There is almost complete absence of lymphoid tissue except around occasional trabeculae. The pulp is occupied by great numbers of erythrocytes, and scattered widely throughout the sections are large amounts of brownish pigment. The most striking feature of this section is the appearance of the splenic sinuses, the lining cells of which present the characteristic arrangement so often found in the spleen of hemolytic jaundice, which gives them the appearance of being arranged in pseudo-acini (Fig. 1 A and B). This appearance is seen throughout the section. *Pathologic Diagnosis:* Typical of the spleen found in cases with hemolytic jaundice

Subsequent Course.—Within one month following the patient's discharge from the hospital he returned to work as a garage mechanic. On April 2, 1935, his blood count showed: Hemoglobin 16.8 Gm., 100.8 per cent, erythrocytes 4,750,000, leukocytes 7,550, no reticulocytes. Hemolysis began at 0.42 and was complete at 0.34. On April 1, 1939, hemoglobin 13.5 Gm., 81 per cent, color index 1.1, erythrocytes 3,630,000, an occasional monoblast was present, leukocytes 6,900. Fragility began at 0.45 and was complete at 0.35. Volume index 1.1.

The patient has not had gallbladder symptoms subsequent to his first admission to the hospital. Oral cholecystography, April 12, 1939, revealed a small, functioning gallbladder, with the shadow of one stone, about 0.8 cm. in diameter, in the fundus.

COMMENT.—During the period of observation of this case microcytosis has not been observed. The critical condition of the patient so strongly indicated repeated transfusions that only two days' observation prior to transfusion was possible.

In the presence of severe anemia and an absence of microcytosis the findings of a normal fragility of the circulating red cells seems plausible. An interesting association between microcytosis and increased fragility is brought out by the observation of Krumbhaar¹⁴ that in various mammals those with the smaller red cells have the higher fragility.

Dawson¹⁵ reports that five of 40 collected cases showed normal fragility of the red cells. Birch and Jaffe¹⁶ report two cases of hemolytic jaundice occurring in adolescence with normal fragility of the red cells and normal reticulocyte counts. Both cases were cured by splenectomy.

Some authors (Cheney and Cheney,¹⁷ and Reynolds¹⁸) have attempted to explain normal fragility on the basis that reticulated red cells are more resistant to hemolysis than normal red cells. While it may be true that reticulated red cells are more resistant than normal, their hypothesis will not explain the normal fragility encountered in the cases of Birch and Jaffe¹⁶ and in the author's case.

It is interesting to note that in the case reported by Reynolds¹⁸ the fragility test was normal, partial hemolysis beginning at 0.4 per cent sodium chloride solution and complete hemolysis at 0.32 per cent. At that time, 95 per cent of the cells showed reticular material.

The cases reported by Baty¹² showed concomitant increased fragility and high reticulocytosis (92 per cent). It appears from a review of the literature that the occurrence of reticular material in the red cells is not the factor responsible for normal fragility when it is encountered.

In the author's case, partial hemolysis of transfused blood was occurring before splenectomy. This was manifested clinically by the increase in the size of the spleen following transfusions, mild reactions, deepening of the jaundice and inability to effect any prolonged increase in the red cell count with frequent large transfusions.

If the spleen becomes overactive in blood destruction function and will destroy normal transfused red cells, it seems plausible to believe that it would rapidly destroy the less resistant red cells as they come into the blood stream and leave circulating the more resistant cells.

Gallstones occur in about 60 per cent of the patients with congenital or acquired hemolytic jaundice. The stones are usually composed almost entirely of the pigment which is present in the bile in great excess. Brooks¹⁸ reports a case of congenital icterus with gallstones in a patient four years old, in whom the spleen was removed and the gallbladder drained. In the author's case there has been, apparently, an almost complete disappearance of the gallstones following splenectomy, as far as is evidenced in the roentgenogram.

In view of the pathologic physiology in these cases with gallstones, it appears rational that biliary tract operations should be reserved for cases of obstruction of the common, hepatic or cystic ducts.

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ACUTE CHOLECYSTITIS PRECEDING NEOPLASTIC COMMON BILE DUCT OBSTRUCTION

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THE PURPOSE of this communication is to report a series of eight cases in which acute cholecystitis occurred during the early course of neoplastic common bile duct obstruction. The cases are interesting in that one can trace the origin of the acute exacerbation of the cholecystitis and can appreciate the factors which led to its development. Also, the cases are of surgical importance in that the underlying malignant lesion was overlooked in every instance because of the acuteness of the gallbladder inflammation.

The patients, consisting of six females and two males, were admitted to the hospital and operated upon because they presented symptoms and signs suggestive of an acute lesion in the biliary tract. All of the patients complained of upper abdominal pain, and in addition, six of them gave a history of belching, pyrosis, and aversion for fatty foods. Similar attacks, dating from one to 25 years prior to hospital admission, had occurred previously in six of the cases. In seven of the patients, the type of pain was characteristic of biliary colic, whereas the eighth patient complained of severe left upper quadrant abdominal pain with radiation to the upper right quadrant and to the back. On admission, the temperature was moderately elevated in all but two cases. The two patients with normal temperature had been suffering from their acute cholecystitis for two weeks and one month prior to hospitalization. Physical examination revealed muscle spasm and tenderness in the right upper quadrant of the abdomen in every instance. Three patients presented tender, palpable gallbladders, but no other abdominal masses were found.

None of the patients had noted jaundice in their previous attacks of cholecystitis, although three of them were definitely icteric on admission. Of the jaundiced patients, two were suffering from their first attack of gallbladder disease. The third had had repeated episodes of pain for ten months but had been jaundiced for only ten days prior to hospitalization.

The preoperative diagnosis in six cases was acute cholecystitis. The other two patients were thought to have obstructive jaundice due to stone or to a carcinoma pressing upon the common bile duct. The operative findings, however, did not seem to substantiate the clinical impression of malignancy in either of these latter two cases. At operation, gangrenous cho-

lecystitis was found in two cases, empyema of the gallbladder in one case, and acute inflammatory cholecystitis in the other five. Cystic duct calculi were encountered in five cases. The other three patients had acute non-calculous cholecystitis.

The operative notes in four cases stated that the common duct and head of the pancreas were free from pathology. In one case, where the omentum was wrapped around a perforating gangrenous gallbladder, no mention was made of the pancreas or common bile duct. One surgeon noted that the pancreatic head was "somewhat enlarged but not the seat of malignancy," and another surgeon found the pancreas to be "soft and edematous." Common bile duct compression by three enlarged lymph nodes was stated as an auxiliary finding in the eighth case. In no instance did the operator suspect that he was dealing with anything but an acute cholecystitis. More complete reports on operative findings will be found in the abstracts of the case records.

Cholecystectomy was performed upon six patients and cholecystostomy upon the other two. A small section of the gallbladder wall was removed from both patients on whom cholecystostomy had been performed. Unfortunately, the microscopic section of the gallbladder of one case could not be located. However, the operating surgeon described the specimen as follows: "Gangrenous gallbladder wall containing frank pus and a few stones." Examination of the microscopic sections in the other seven cases revealed an acute cholecystitis, in most instances superimposed upon chronic inflammation. None of the gallbladders showed any neoplastic tissue. The pathologic reports are given in detail in the abstracts of the case records, and photomicrographs of sections of the gallbladder wall will be found elsewhere in this report.

Seven of the eight patients recovered from the gallbladder operation, although convalescence was complicated in four instances. It is interesting to note that the operative findings in the three patients who had the most uneventful postoperative courses stated that the pancreas and common duct were normal. Evidently the compression of the common bile duct by the growing neoplasm was not yet great enough to retard operative recovery. A right hemiplegia developed in one patient on the tenth postoperative day, but the course was otherwise uncomplicated and the patient eventually became well enough to be discharged from the hospital. One patient, upon whom cholecystostomy had been performed, failed to drain sufficient bile, probably because the acute inflammation had caused a temporary blocking of the cystic duct. She was able to leave the hospital after 15 days of postoperative convalescence, but still showed a moderate icterus and inadequate biliary drainage. Two patients who had been subjected to cholecystectomy ran a markedly febrile course but managed to attain operative recovery after developing biliary fistulae. The eighth patient died three days following cholecystostomy for an empyema of the gallbladder. In this case, the underlying malignant lesion was unexpectedly discovered at autopsy.

The histories of the interval course, from the time of hospital discharge to readmission, bore great similarities. Weakness, anorexia and weight loss occurred in all cases. No patient made a sufficiently complete recovery so that he or she could return to the performance of normal duties. Case 1 developed jaundice a few days after discharge from the hospital and continued with symptoms of biliary disease for the 13½ weeks between hospitalizations. Case 2 became jaundiced ten weeks following discharge from the hospital and was readmitted in the middle of the thirteenth week. Case 3 continued to have abdominal pain and other preoperative symptoms for the entire interval of 11 weeks, from the time of the first discharge to second admission to the hospital. Case 4 also failed to have symptomatic relief following the gallbladder operation and was readmitted to the hospital ten weeks later. Case 5 showed progressive weight loss, anorexia, and weakness during her interval period. The biliary fistula continued to drain, but icterus continued and the patient was forced to seek readmission to the hospital 24 weeks after her first discharge. Case 6 came back to the hospital two weeks following her discharge. She had had chills, fever, and abdominal pain throughout the entire interval. Case 7 developed a postoperative biliary fistula and maintained a fair state of health for the first 12 weeks after leaving the hospital. He then developed jaundice which receded spontaneously after two weeks. Readmission to the hospital, 20 weeks after his first discharge, was necessitated by a second recurrence of jaundice. (As previously mentioned, Case 8 died three days following first operation.) In six of the above seven cases, the appearance of jaundice was the deciding factor which led to readmission to the hospital. The nonicteric patient was readmitted with a diagnosis of subhepatic abscess.

On second admission, all of the patients looked chronically ill. There were none of the acute findings of abdominal tenderness and muscle spasm which had been present on previous examination. An abdominal mass in the region of the scar of the gallbladder operation could be palpated in three of the seven cases. The clinical impression in six cases was common bile duct obstruction. Carcinoma of the head of the pancreas or bile ducts was considered as the cause of obstruction in five of these cases, although common duct stone or common duct stricture was also mentioned as a possible diagnosis. The sixth case was thought to have a calculus which had been overlooked at the previous operation, and the seventh patient was diagnosed preoperatively as having a subhepatic abscess.

A markedly enlarged, firm, nodular head of the pancreas was found at operation in four cases. A mass arising from the region of the common bile duct was discovered in two cases. The underlying malignant lesion was found in the two remaining cases at autopsy. The pathologic specimens of malignancy were obtained by biopsy at operation in four cases, whereas, three other specimens were obtained only at autopsy. Thus, there is but one case in which no microscopic section is available, and in that case, the operating

surgeon stated that the head of the pancreas was markedly enlarged, hard and nodular, with enlargement extending up along the common duct.

The three pathologic specimens obtained from the common bile duct showed typical carcinoma. The three specimens removed at operation from the head of the pancreas or peripancreatic lymph nodes also showed typical carcinoma. The sections from the seventh patient showed a rhabdomyosarcoma which had originated in the upper end of the right iliopsoas muscle and had metastasized widely. Autopsy revealed that the head of the pancreas was infiltrated with metastatic tissue and was surrounded by large, pale-gray and pale-yellow lymph nodes which, microscopically, also showed sarcoma. The terminal end of the common bile duct had been constricted by these metastatic nodes. Detailed pathologic reports as well as photomicrographs of all specimens are to be found with the abstracts of the case records.

ABSTRACTS OF CASE RECORDS

Case 1.—Hosp. No. 73409: S. S., white, female, age 52, was admitted to the hospital July 7, 1922, because of excruciating pain in the right hypochondrium, nausea, vomiting and constipation. Pain radiated to right shoulder and around to the back. History of many similar attacks, relieved only by injection of morphine during past 11 years. No jaundice. Physical examination revealed marked tenderness in right upper quadrant of abdomen with a tender, palpable gallbladder. A preoperative diagnosis of acute cholecystitis was made, and the patient was operated upon the day following admission.

Operative Pathology.—Gangrenous, distended gallbladder containing a few stones and frank pus. No adhesions to surrounding structures. No other pathology noted.

Procedure.—Cholecystectomy.

Patient made an uneventful recovery and was discharged on the eighteenth postoperative day, July 26, 1922.

Within a few days after leaving hospital, the patient began to have pruritus and noticed that her urine was dark in color. Soon thereafter, the family noticed that her skin was "yellow." Two months following discharge from hospital, nausea and vomiting recurred, but no colicky pain. There were steady loss of weight, anorexia, and weakness from the time of gallbladder operation until readmission to the hospital. Patient was readmitted, October 28, 1922, because of the progressive jaundice, weight loss, weakness and vomiting. Physical examination revealed skin to be markedly icteric. Scar in right upper quadrant well healed, no palpable masses. The clinical impression was that the patient was suffering either from constriction of the common bile duct by adhesions, or that a malignancy was present. The second operation was performed, November 3, 1922.

Operative Pathology.—Dense adhesions at site of previous cholecystectomy. Very dark cholemic liver. Indurated enlarged pancreas. Induration along common bile duct. Pancreas of stony hardness producing pressure on common bile duct. No calculi palpable.

Procedure.—Tissue excised from head of the pancreas and along common bile duct.

Pathologic Examination.—The tissue is composed of nests and cords of large cylindric cells varying in size, shape and staining reaction of the nuclei. Many are in mitotic division. In some areas, they form lumina which are widely distended with amorphous, lavender-staining material. In places, tumor tissue is seen within distended endothelial lined spaces. The stroma is abundant, loose and densely infiltrated with small and large mononuclear cells, eosinophils and polymorphonuclear leukocytes. Deposits of calcium are seen at one end of the section. In some areas, too, the lumina are large and are lined by compressed cells. Within such lumina, there are amorphous lavender-staining material and groups of tumor cells (Fig. 1). *Pathologic Diagnosis:* Adenocarcinoma (colloid).

Postoperatively, the patient did poorly. A biliary fistula developed on the fifth day after operation. The patient was finally discharged from the hospital on the sixtieth post-operative day in poor condition, deeply jaundiced.

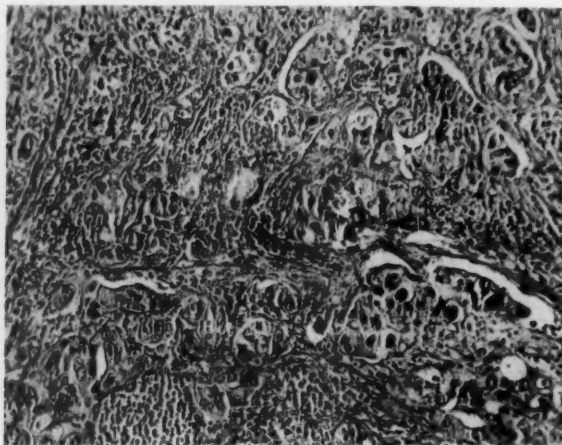


FIG. 1.—Path. No. A1088: Photomicrograph showing carcinomatous tissue removed from the head of the pancreas. ($\times 250$)

Case 2.—Hosp. No. 123590: J. B., white, female, age 58, was admitted to the hospital, October 6, 1929, complaining of right upper quadrant abdominal pain for past two weeks. Pain was severe and colicky and caused patient to double up. Nausea, chilly sensations and fever accompanied this attack which recurred several times during the days

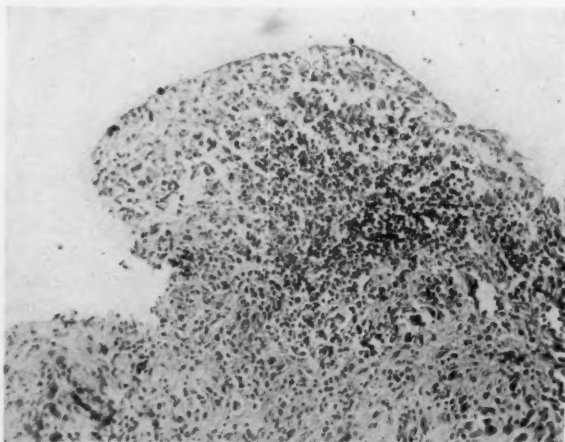


FIG. 2.—Path. No. 22113: Photomicrograph showing portion of wall of gangrenous gallbladder. ($\times 250$)

preceding hospitalization. History of abdominal bloating, belching and pyrosis for many years. No jaundice or clay-colored stools. Physical examination showed tenderness and muscle spasm in right upper quadrant of abdomen. Gallbladder was palpable as a tender mass just below the right costal margin. A preoperative diagnosis of an acute exacerbation of a chronic cholecystitis was made.

Operation.—Cholecystectomy was performed, October 9, 1929.

Operative Pathology.—Gallbladder was three times normal size, full of calculi, con-

ACUTE CHOLECYSTITIS AND CANCER

taining small amount of pus. Apparent perforation of gallbladder into liver bed. Surrounding liver tissue edematous, boggy, and covered with a plastic exudate. Gallbladder itself embedded in massive adhesions and covered with omentum. Cystic duct edematous and compressed by a large lymph node. Moderate degree of neighboring duodenitis. *Operative Diagnosis:* Gangrenous cholecystitis.

Pathologic Examination.—Destruction of the mucosa and necrotic tissue in the wall of the gallbladder which is the seat of areas of polymorphonuclear cell infiltration, edema and extravasation of blood (Fig. 2). *Pathologic Diagnosis:* Acute suppurative cholecystitis with gangrene.

Postoperative course was satisfactory until the tenth day when patient suddenly became unconscious and developed paralysis of right arm and right leg. Consciousness eventually returned and patient was found to have a motor aphasia. The abdominal wound healed and patient was discharged from hospital on the thirty-fifth day after operation.

Subsequent Course.—Ten weeks following hospital discharge, pruritus and jaundice appeared. On readmission, February 9, 1930, the patient was found to be deeply jaundiced and to have acholic stools. No abdominal pain during interval between hospital discharge and readmission. Except for the residual signs of the hemiplegia and the deep jaundice, physical examination revealed no significant findings. Abdomen was soft and flat; no masses palpable. *Preoperative Diagnosis:* Common duct obstruction, due either to stricture secondary to previous cholecystectomy or to malignancy. The second operation took place ten days following readmission, February 19, 1930.

Operative Pathology.—No free fluid in peritoneal cavity. Liver slightly enlarged, congested, showing evidence of biliary cirrhosis. Duodenum and pylorus firmly adherent to liver in region of portal fissure. A marked cartilaginous cicatrix at the upper part of the common duct just below the junction of the cystic duct was found. No evidence of suppuration. Head of pancreas moderately enlarged, but no evidence of neoplastic pathology.

Procedure.—Adhesions between liver, pylorus, duodenum and common duct separated. A portion of tissue which was involved in the cicatrix about the common duct was excised, thus releasing some of the constriction on the common duct. Rubber dam inserted in Morrison's pouch.

Pathologic Examination.—Specimen is an ovoid mass of tissue 4 cm. in diameter. Examination shows tissue to be made up of carcinomatous masses, the cells of which appear to be highly malignant (Fig. 3).

Postoperatively, the patient did very poorly, despite intermittent drainage of bile through the abdominal wound. Cholemia became marked. Patient was discharged from hospital, deeply jaundiced, in poor condition, on the forty-eighth day following operation.

Case 3.—Hosp. No. 184215: N. M., white, female, age 47, was admitted to the hospital, October 1, 1935, because of very severe recurrent epigastric pain, epigastric distress, belching, anorexia and weight loss of one year's duration. Pain much worse during the five months previous to admission. The epigastric pain radiated to the back. Roentgenograms, taken prior to admission, revealed calculi in the gallbladder.

Physical Examination.—Spasticity and tenderness in the right upper quadrant; no masses palpable. No jaundice. A preoperative diagnosis of subacute cholecystitis and cholelithiasis (acute exacerbation of chronic cholecystitis) was made and the patient operated upon on the third hospital day.

Operative Pathology.—Acutely inflamed, distended gallbladder, opaque, about three times normal size, with moderately thickened walls. Numerous adhesions between gallbladder and surrounding structures. A large stone was impacted at the junction of the ampulla and cystic duct. No pathology noted along the common duct, in the pancreas or duodenum.

Procedure.—Cholecystectomy.

Pathologic Examination.—The mucosal coat is markedly hypertrophied. There is an increase of the intermuscular and perimuscular connective tissue. All the layers are somewhat edematous and in areas show freshly extravasated blood. An infiltration

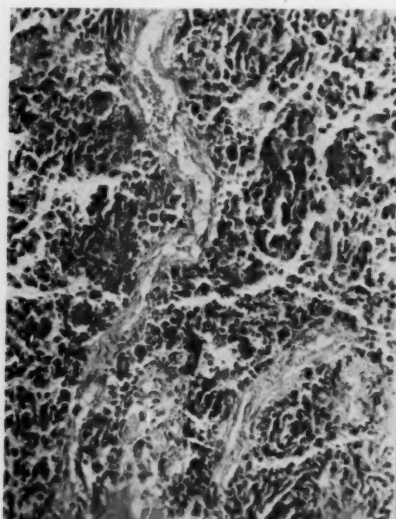


FIG. 3.—Path. No. 23285: Photomicrograph showing carcinoma of the common bile duct. ($\times 250$)

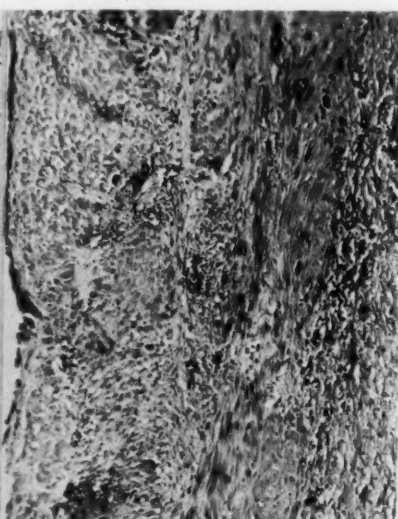


FIG. 4.—Path. No. 982: Photomicrograph showing a portion of the gallbladder wall involved in an acute inflammatory process. ($\times 180$)

of polymorphonuclear leukocytes and large mononuclear cells is seen in the tunica propria, in the intermuscular connective tissue and the perimuscular connective tissue (Fig. 4).
Pathologic Diagnosis: Acute and chronic cholecystitis.

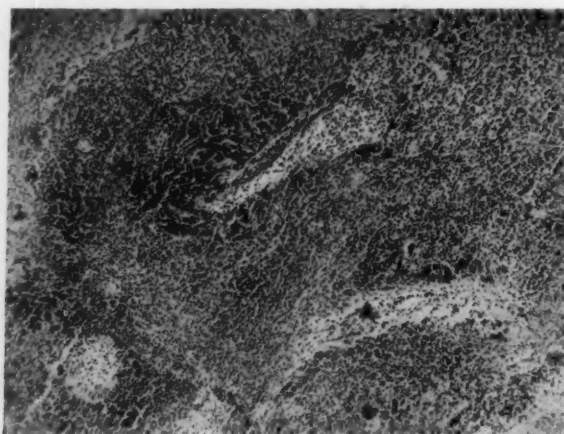


FIG. 5.—Path. No. 2112: Photomicrograph showing peripancreatic lymph node with metastatic carcinoma. ($\times 170$)

Patient made an uneventful recovery and was discharged on the seventeenth post-operative day, October 19, 1935.

Subsequent Course.—Immediately upon leaving the hospital, the patient experienced recurrent pains of the same nature as those experienced previous to operation. Loss of

weight continued and patient vomited occasionally. Patient was readmitted, January 2, 1936, three months after being discharged, with continuous severe epigastric pain radiating to the back. Physical examination revealed a markedly emaciated woman, jaundiced. Scar of previous operation well healed, with a mass the size of an egg running from its upper one-third toward the midline. Clinical impression was a carcinoma of the head of the pancreas. Patient was reoperated upon, January 4, 1936.

Operative Pathology.—A hard, nodular mass about the size of a small grapefruit, involving the entire pancreas from head to tail.

Procedure.—A small, hard node situated over the head of the pancreas was taken for biopsy.

Pathologic Examination.—Peripancreatic lymph node with metastatic carcinoma (Fig. 5).

Postoperatively, the patient did poorly, became even more jaundiced, but recovered sufficiently to leave the hospital on the seventeenth postoperative day.

Case 4.—Hosp. No. 181636: E. Z., white, female, age 56, was admitted to the hospital, June 17, 1935, complaining of right upper quadrant abdominal pain with radiation to back and right shoulder, on and off for past four weeks. Pain most severe after meals and accompanied by belching. Morphine given on several occasions to relieve attacks of colic. No jaundice or acholic stools. Occasional similar attacks during past five years. Cholecystostomy had been performed 24 years ago for cholelithiasis. Typhoid fever as a child. Thyroidectomy six years before present admission. Physical examination revealed rigidity in both upper abdominal quadrants, most marked on the right side. Tenderness on pressure over region of gallbladder beneath right costal margin. *Preoperative Diagnosis:* Acute exacerbation of chronic cholecystitis.

Operative Pathology.—An inflamed gallbladder in a maze of adhesions. The ampulla was in close proximity to the second portion of the duodenum and there was marked pericholecystitis. A large ovoid stone was impacted in the cystic duct. Some cirrhosis of liver. The rest of the alimentary tract was apparently negative.

Procedure.—Cholecystectomy.

Pathologic Examination.—Gallbladder wall dull and granular. Wall moderately thickened. Serosa is thickened and fibrous; muscularis hypertrophied, and wall is infiltrated with plasma cells, mononuclear cells, and some polymorphonuclear leukocytes. Mucosa is diffusely ulcerated (Fig. 6). *Pathologic Diagnosis:* Chronic and acute cholecystitis. Ulcerative cholecystitis.

The postoperative course was satisfactory except for a notation on the chart on the tenth day stating that there was slight icterus. Patient discharged in good condition with wound healed on fourteenth day following operation, July 2, 1935.

Subsequent Course.—The pain in right upper quadrant with radiation to the back persisted after patient was discharged and continued until readmission, September 9, 1935. No jaundice. Hospitalization was advised solely because of the persistent pain, and it was the impression that a common duct stone had been overlooked at the first operation, or that a malignancy was present. The preoperative diagnosis on the operative sheet was "carcinoma of the stomach (?)."

Operative Pathology.—Stomach, duodenum and intestines normal. Numerous adhesions about the gallbladder bed. Common duct was exposed and found to be dilated. Stump of the cystic duct was distended and contained débris and several calculi. The pancreas was markedly enlarged from the head extending down toward the tail.

Procedure.—Biopsy of tissue from region of head of pancreas taken. Choledochotomy performed and clear bile aspirated. A large T-tube was inserted into the common duct.

Pathologic Examination.—Specimen consists of tissue measuring 2x2x1.5 cm., irregularly lobulated, gray and pink. Tissue said to come from pancreas. Sheets of epithelial cells are imbedded in a scant hyalinizing fibrous connective tissue stroma, densely infiltrated with round cells, mononuclear cells and polymorphonuclear leukocytes. The

peripheral cells have a palisade arrangement. The nuclei are large, vesicular, hyperchromatic, and an occasional mitotic figure is seen (Fig. 7). *Pathologic Diagnosis:* Carcinoma, metastatic.

Postoperatively, the patient had a satisfactory course, drained bile, and was able to leave the hospital on the eighteenth day after operation.

Case 5.—Hosp. No. 191379: M. M., white, female, age 58, entered the hospital, May 25, 1936, because of cramp-like abdominal pain, nausea and vomiting which had begun 16 days previously. Two or three days following onset of pain, urine became dark in color, stool gray, and skin jaundiced. Two or three days prior to admission, the icterus appeared to be less intense. Past history was entirely negative for previous similar attacks. Physical examination revealed a thin, undernourished woman, lying comfortably in bed. There was moderate tenderness and muscle spasm in the epigastrium



FIG. 6.—Path. No. 812A: Photomicrograph showing area of acute inflammation in gallbladder wall. (X200)

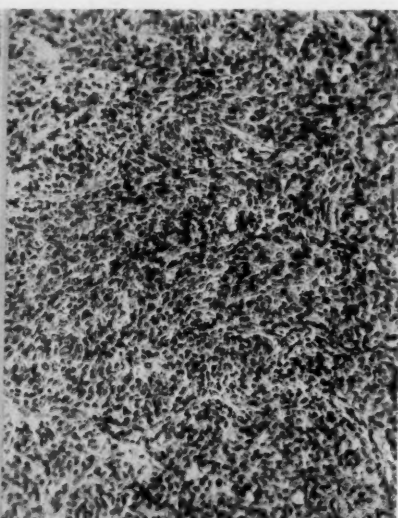


FIG. 7.—Path. No. 812B: Photomicrograph of a biopsy taken from the region of the head of the pancreas showing diffuse carcinoma. (X290)

and right upper quadrant of abdomen. A rounded, tender mass, the size of a man's fist, was palpated three fingers' breadth below the right costal margin. A preoperative diagnosis of obstructive jaundice due to common duct stone was entertained and the patient was operated upon the day following entrance into the hospital.

Operative Pathology.—Moderately distended gallbladder showing evidence of acute inflammation. No evidence of any neoplasm or calculi. There was a moderately enlarged head of the pancreas which did not give the impression of malignancy. Digestive tract normal. *Postoperative Diagnosis:* Acute cholecystitis, chronic pancreatitis.

Procedure.—Cholecystostomy. Portion of gallbladder wall taken for microscopic examination.

Pathologic Examination.—Specimen consists of soft, gray tissue, 1.2x1x0.6 cm. in diameter. Part of the mucosal surface is thrown into folds covered by cylindric cells. There is a marked increase of connective tissue of the tunica propria as well as of the intermuscular and perimuscular connective tissue. These are infiltrated with extravasated blood, small round cells, large mononuclear cells and polymorphonuclear leukocytes (Fig. 8). *Pathologic Diagnosis:* Acute and chronic cholecystitis.

Postoperative course was fairly satisfactory, although for the first few days there

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was rather little bile drainage. The wound healed and the patient was discharged with a biliary fistula on the fifteenth day after operation, June 10, 1936. On the day prior to discharge, temperature rose to 104° F., but returned to normal within a few hours.

Subsequent Course.—Drainage of greenish bile through the abdominal fistula persisted following discharge from the hospital. Weakness and loss of 21 pounds in weight occurred during the interval. At no time, from discharge on June 10 to readmission on November 22, did the patient regain normal or approximate normal health. Stools were constantly clay-colored. The patient returned to the hospital because of persistent, slight icterus and continued weight loss. She appeared emaciated, but otherwise no significant physical findings were observed. No abdominal masses palpable. Fistula was lined by granulation tissue and was draining bile. Operation was deemed advisable be-

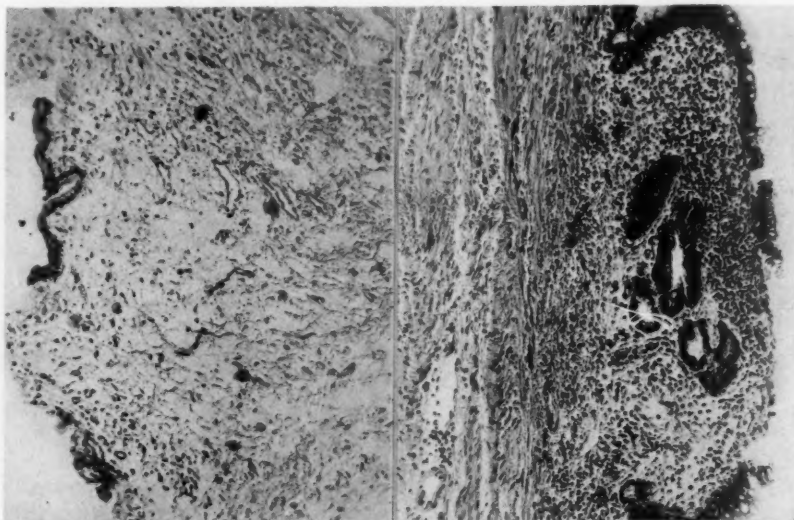


FIG. 8.—Path. No. 4010: Photomicrograph showing acute cholecystitis. (×200)

FIG. 9.—Path. No. 5697: Photomicrograph showing acute inflammation of the gallbladder wall. (×270)

cause it was thought that a common duct stone had been overlooked at the first operation or that a malignancy of the head of the pancreas was present.

Operative Pathology.—Numerous pericholecystic adhesions. Foramen of Winslow partially patent. A large, nodular head of the pancreas with a prolongation upward along the common duct was felt. Common duct contained no calculi. *Postoperative Diagnosis:* Carcinoma of head of the pancreas.

Procedure.—Cholecystoduodenostomy.

The patient made a satisfactory operative recovery. Bile did not drain through the wound and icterus decreased. Stools began to show bile, thereby demonstrating a functioning cholecystoduodenostomy. Patient left hospital on the seventeenth postoperative day.

Case 6.—Hosp. No. 195095: D. B., white, female, age 46, was admitted to the hospital, September 30, 1936, because of severe colicky right upper quadrant abdominal pain of two days' duration. Pain radiated to the back and was associated with nausea and vomiting. Temperature had been elevated to 102° F., and there had been several chills. Belching and aversion for fatty foods for many years. Physical examination showed an acutely ill patient complaining of abdominal pain. Muscular spasm and marked tenderness in the epigastrium and right upper quadrant of the abdomen was noted. No masses. No jaundice or history of jaundice. A diagnosis of acute exacerbation of a chronic

cholecystitis was made and the patient was subjected to surgery on the second day after admission.

Operative Pathology.—Large, tense distended gallbladder with thickened wall, partially embedded in liver substance. There appeared to be anomalous vessels arising from the cystic artery. A stone was found impacted in the cystic duct. Common duct and head of pancreas appeared normal. No other pathology noted.

Procedure.—Cholecystectomy. An excess amount of bleeding was encountered during the operation.

Pathologic Examination.—The mucosal surface is thrown into folds covered with tall columnar cells. There are in places invaginations of the mucosa which extend to the somewhat hypertrophied muscular coat. The lamina propria is broadened by edema and is infiltrated by small round cells, large mononuclear cells, some eosinophils and polymorphonuclear leukocytes. A similar cellular infiltration, though less marked, is seen in the intermuscular and perimuscular connective tissues. In the latter, some vessels show margination of white blood cells and there are small foci of extravasated blood (Fig. 9).
Pathologic Diagnosis: Acute and chronic cholecystitis.

Postoperatively, the patient did poorly. Temperature remained high with daily elevations to 102° F. The wound became infected and drained thin, gray pus and bile. However, from the eleventh to the fourteenth day, the temperature subsided and the patient was considered sufficiently recovered to discharge, October 18, 1936.

Subsequent Course.—On the day following discharge, temperature rose to 104° F. A deep abscess was evacuated from area in wound at the site of the drain. A small amount of bile drained for the next two to three days, but stopped spontaneously. Temperature, anorexia and malaise continued despite drainage of the wound abscess. A mass in the right upper quadrant of the abdomen extending down toward the right iliac spine was palpated. The patient was readmitted two weeks following discharge. It was thought that a subhepatic abscess was in process of formation but that operation should be deferred until further localization had occurred. The patient was observed for the next four weeks, during which time she became progressively weaker, lost weight, and ran a temperature ranging from 102° to 104° F. The abdominal mass became larger, but instead of localizing, it appeared to become more diffuse. On December 4, 1936, an oblique incision in the right flank was made.

Operative Pathology.—No pus was found. Exploration of the retroperitoneal space revealed a markedly enlarged right kidney with induration of the perirenal fat, and boggy-ness and thickness extending up above the kidney and toward the liver, and retroperitoneally below the kidney down along the course of the iliopsoas muscle. *Postoperative Diagnosis:* Retroperitoneal phlegmon.

Procedure.—Insertion of rubber drains.

The patient responded very poorly to operation. Despite blood transfusion and other supportive measures, the patient went into shock and expired the day following operation.

Autopsy.—Sarcoma of iliopsoas muscle, right; metastasis to regional, abdominal, retroperitoneal, axillary lymph nodes, spleen, pancreas, ovary, peritoneum, ureters, thyroid, and to the vertebrae. The pancreas measured 21x4x2 cm., weighed 120 Gm., and showed sarcomatous metastases. The head of the pancreas was surrounded by large, pale-gray lymph nodes measuring up to 3x3 cm. in size (Fig. 10).

Case 7.—Hosp. No. 216288: S. A., white, male, age 46, was admitted to the hospital, February 26, 1938, because of colicky right upper quadrant abdominal pain and nausea, particularly severe the past ten days. He had noticed anorexia, aversion for fats, weight loss and weakness for the past month. Six years ago, he had had a right hemicolectomy for carcinoma of the ascending colon. His health had been excellent since then and his bowel function had been normal. For ten days prior to admission, his skin became jaundiced and pruritus marked. Physical examination revealed jaundiced skin and evidence of marked weight loss. Liver was enlarged to two fingers' breadth below the right costal margin. Tenderness was extreme in the gallbladder area, with moderate

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muscle rigidity. No other masses palpable. *Preoperative Diagnoses:* (1) Metastases to liver secondary to carcinoma of colon; or (2) acute cholecystitis with cholelithiasis and common bile duct obstruction. Operation was performed, March 15, 1938.

Operative Pathology.—Omentum intimately adherent to the anterior parietal wall and gallbladder. Gallbladder was enlarged, firm, distended and noncompressible. Wall was injected, opaque, thickened and edematous. Lumen contained light mucobile and no calculi. Cystic and common ducts were normal to palpation. Liver enlarged to two fingers' breadth below costal margin; the surface was smooth and no nodules were noted. Pancreas and duodenum normal. Adjacent to the common duct, three distinct soft nodes the size of almonds, not exerting pressure on the common duct, were noted. *Postoperative Diagnosis:* Acute cholecystitis, noncalculous.

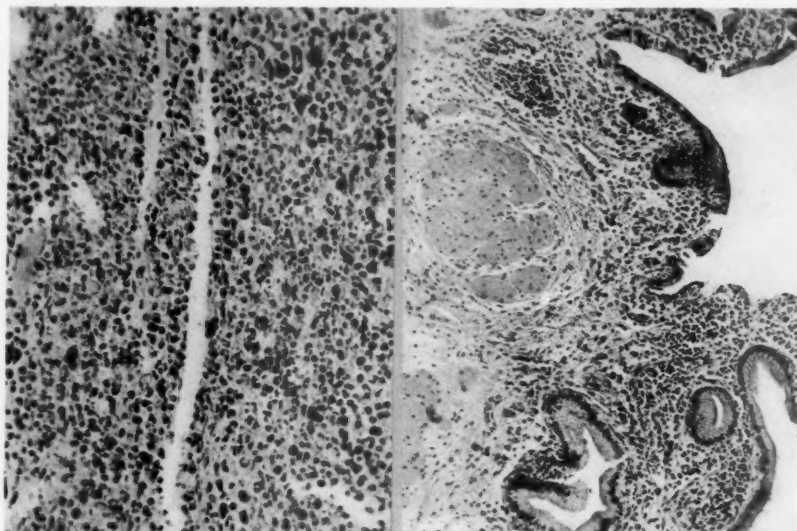


FIG. 10.—Path. No. 2798: Photomicrograph showing rhabdomyosarcoma; section taken from upper end of right iliopsoas muscle. ($\times 280$)

FIG. 11.—Path. No. 810: Photomicrograph showing acute cholecystitis. ($\times 270$)

Procedure.—Cholecystectomy.

Pathologic Examination.—The mucosal surface of the gallbladder is thrown into coarse and delicate folds. There are occasional infoldings of the epithelium extending into the greatly hypertrophied muscular coat. Connective tissue of the tunica propria is greatly increased in amount and is infiltrated with small and large mononuclear cells, eosinophils, plasma cells and polymorphonuclear leukocytes. This cellular infiltration is also seen in the intermuscular and perimuscular connective tissue. Some of the blood vessels show margination of the white blood cells. A similar infiltration is also seen in the serosa which is broadened by edema (Fig. 11). *Pathologic Diagnosis:* Acute and chronic cholecystitis.

The patient did fairly well postoperatively for the first two weeks. Jaundice slowly cleared and the wound healed, despite a large hematoma and wound infection. On the twenty-second day after operation, the patient developed a spontaneous biliary fistula which drained large quantities of bile. His course was further complicated by a diffuse pyoderma caused by *Staphylococcus aureus*. He was kept in the hospital for 69 days after operation, during which time his biliary sinus drained intermittently. *Staphylococcus* vaccine was given in large quantities to control his diffuse, pustular skin eruptions.

Subsequent Course.—From the date of discharge, May 23, until August 20, he was

evidently in fairly good health. However, his biliary fistula then stopped draining and he became jaundiced. This lasted for two weeks and subsided spontaneously. He developed jaundice again, September 26, which persisted until readmission to the hospital, October 10. The day prior to hospitalization, he suffered moderate right upper quadrant abdominal pain and had a temperature of 102° F. Physical examination revealed slight tenderness in the region of the scar in the right upper quadrant but no masses. A pre-operative diagnosis of common duct stone was made. The patient was treated conservatively in an attempt to better prepare him for the surgical procedure. He was operated upon, November 8, 1938.

Operative Pathology.—The common duct was found markedly dilated. It was opened and probed in both directions but no calculi were found. The duodenum was then opened and the common duct explored through the papilla of Vater but still no stones were found. The duodenum was closed and a T-tube inserted into the common duct. Postoperatively, the patient developed a duodenal fistula, went downhill rapidly, and died on the sixth day after operation.

Autopsy.—A carcinoma was found which originated in the terminal end of the com-

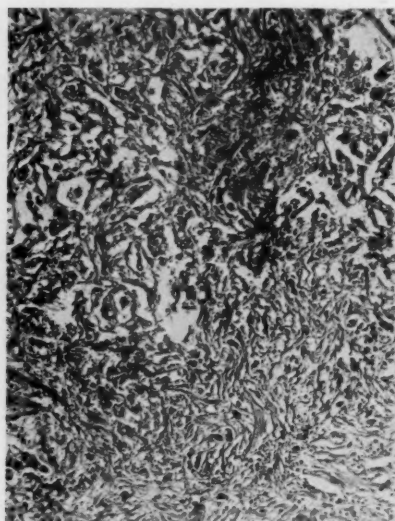


FIG. 12.—Path. No. 38-165: Photomicrograph showing section of carcinomatous tissue from the common bile duct. ($\times 180$)

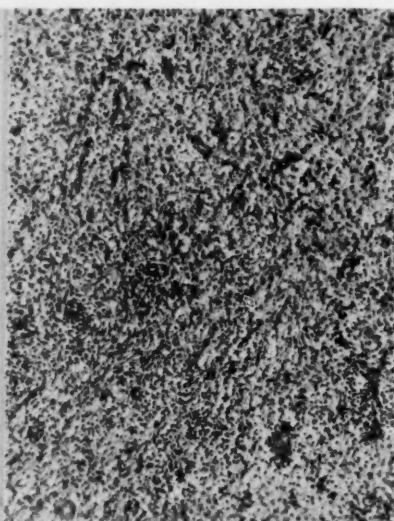


FIG. 13.—Path. No. 2974: Photomicrograph showing acute inflammatory process in wall of gallbladder. ($\times 195$)

mon bile duct and extended into the duodenum. There were metastases to regional lymph nodes. The duodenum was perforated at the site of its incision with a resultant retroperitoneal cellulitis and areas of fat necrosis. No pathology was noted at the site of anastomosis of the ileum to the transverse colon (Fig. 12).

Case 8.—Hosp. No. 215187: H. T., white, female, age 68, was admitted to the hospital, September 13, 1938, complaining of constant upper abdominal pain, anorexia and weight loss of two months' duration. Icterus and pruritus noted for past two weeks. For about one year patient had been having attacks of cramp-like left upper quadrant pain radiating to the epigastrium, the right upper quadrant and around to the back. Physical examination revealed cachexia, jaundice, and voluntary upper abdominal muscle spasm. No masses palpable. A clinical diagnosis of either carcinoma of the head of the pancreas or common bile duct calculus was made, and the patient was operated upon, September 24, 1938.

Operative Pathology.—An inflammatory mass including the omentum, transverse

colon, ileum and gallbladder was encountered. Pancreas slightly enlarged but not firm or nodular. The gallbladder, after being released from the surrounding adhesions, was found to be grayish-yellow; the wall was necrotic and considerably thickened. In the lumen, yellow, purulent material was present. No stones found either in gallbladder or cystic duct. Common duct not visualized because of adherent surrounding tissues. The liver extended three fingers' breadth below the costal margin. *Postoperative Diagnosis:* Empyema of the gallbladder.

Procedure.—Cholecystostomy. A small portion of the gallbladder wall was taken for microscopic study.

Pathologic Examination.—The mucosal surface is completely missing. The wall is greatly thickened. In places it is densely infiltrated by many small round cells, large mononuclear cells, plasma cells and some polymorphonuclear leukocytes. Numerous thin-walled capillaries distended with blood are seen scattered throughout the entire wall. No

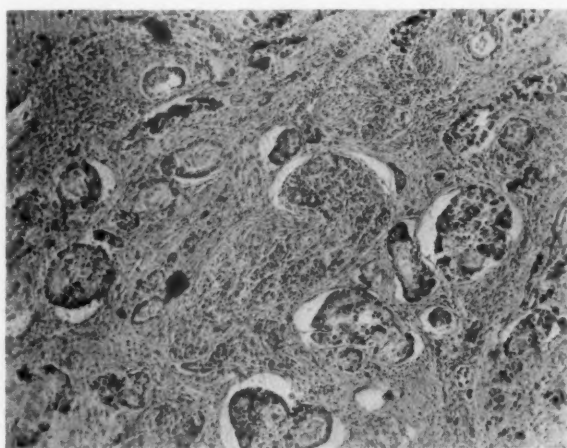


FIG. 14.—Path. No. 38-142: Photomicrograph showing section of carcinomatous tissue from common bile duct. ($\times 115$)

neoplastic cells seen (Fig. 13). *Pathologic Diagnosis:* Acute and chronic inflammation of gallbladder.

The patient went rapidly downhill, and expired three days following operation.

Autopsy.—At its junction with the cystic duct, the common duct shows a circular, gray, firm mass, 2 cm. in width and 3 cm. in length. The lumen at this point shows a granular surface and its caliber is narrowed so that escape of bile is obstructed. Microscopic examination of tissue from common bile duct shows the surface to be composed of folds of necrotic tissue in which ghosts of cell structures are seen. There are acinar and duct-like structures lined by low cuboidal and cylindric cells which vary in size, shape and chromatin content of their nuclei. Occasional mitotic figures are seen. Many of the lining cells project beyond the basement membranes into the surrounding fibrous tissue. Clumps of cells are also seen within endothelial-lined spaces. The cytoplasm of these cells is predominantly abundant and finely granular. The nuclei are either vesicular, round or dark staining and bizarre-shaped (Fig. 14). *Pathologic Diagnosis:* Carcinoma of common bile duct.

COMMENT.—Seventy-three patients with carcinoma of the head of the pancreas and 17 patients with carcinoma of the common bile duct entered the hospital from 1913 to 1938.* Of these 90 patients, 19 had cholecystitis,

* Unpublished data, Jewish Hospital, Brooklyn, N. Y.

as proved either by operation or roentgenographic evidence of a nonfunctioning gallbladder. Seven of the eight cases of acute cholecystitis, herein reported, are part of this group of 19 cases.

As the majority of patients who develop carcinoma of the head of the pancreas or common bile duct give no history of preceding gallbladder infection, this factor has been considered of little etiologic significance. Ransom,¹ in a thorough review of 89 operative cases of carcinoma of the head of the pancreas and extrahepatic bile ducts, found antecedent gallbladder pathology in 15. Rives, Romano and Sandifer² encountered gallbladder pathology in eight of their 96 patients with carcinoma of the pancreas. Eusterman and Wilbur³ found that six of 88 nonjaundiced patients with carcinoma of the pancreas also had gross cholecystitis. Marshall⁴ reported that 26 of his 49 patients with carcinoma of the extrahepatic bile ducts had gallbladder disease. None of these authors suggests that the cholecystitis played an important etiologic rôle, although all mention the possibility of some causal relationship.

The high incidence of gallbladder disease observed in our cases may possibly be attributed to the fact that biliary infection occurs so frequently in Jewish people. It is interesting to note that 18 of the 19 patients with antecedent cholecystitis were Jewish. Furthermore, although carcinoma of the pancreas is twice as common in men as in women, we find that there are more women than men in the group with a preceding cholecystitis. This is explained by the fact that cholecystitis has a much greater incidence among women.

We agree with the authors quoted, that cholecystitis probably plays an unimportant rôle in the etiology of a neoplasm of the common duct or head of the pancreas. However, it has long been recognized that disturbances in tissue tension resulting from a surgical procedure can accelerate the growth of a neoplasm. As the time interval between the acute cholecystitis and the discovery of the malignancy was so short in our series of cases, one might hypothesize that the gallbladder infection caused the underlying tumor to grow with inordinate rapidity. Conversely, it is reasonable to assume that the presence of a malignant lesion permitted the infectious process in the gallbladder to take a firmer hold than it would have under ordinary circumstances.

Scant consideration has been given to the subject of *acute* cholecystitis as a lesion occurring during the early course of carcinoma of the pancreas or common bile duct. Ransom's allusion to a case of empyema of the gallbladder in a patient with carcinoma of the head of the pancreas was the only instance we encountered in reviewing the literature. Since chronic cholecystitis has been noted so frequently as an antecedent condition in neoplasms of the common duct and head of the pancreas, we feel that it is only natural to expect that a certain number of these cases will be complicated by an acute cholecystitis. Furthermore, all of the factors which would cause a chronic cholecystitis to become an acute cholecystitis are present in the

eight cases which we have described in this report. Thus, biliary stasis was increased because of the compression of the common duct by the neoplasm; intraductal pressure became greater due to interference with free biliary drainage; the blood supply to the gallbladder wall may have been embarrassed by pressure from the enlarging head of the pancreas or tumor in the common duct; and the cystic artery or cystic veins might have been compressed by enlarged lymph nodes or by surrounding edema.

Infection finds a fertile soil for taking root in the presence of stasis, increased intraductal pressure and partial common duct obstruction. If there has been a preexistent chronic infection of the gallbladder, it is even easier for reinfection to take hold. When one or more of these phenomena occurs, an otherwise quiescent chronic cholecystitis may become markedly acute. A cystic duct stone, which had previously produced only partial block, may cause complete obstruction with subsequent empyema or gangrene. An exacerbation of a chronic cholecystitis may be precipitated by edema of the neck of the gallbladder, insufficient blood supply, or venous congestion resulting from impingement by the neoplasm. It is our opinion that such was the sequence of events in these eight cases.

The short interval, varying from a few days to 12 weeks, between the operation for acute cholecystitis and the development of symptoms of the underlying malignancy, suggests that the neoplasm must have been present at the time of the first operation. It is hardly conceivable that the malignancy could have developed in such a short space of time. In retrospect, we find that indications of the underlying tumor were present at the first operation in several of the cases, but that the severity of the acute findings led to the misinterpretation of these clues. Edema and enlarged lymph nodes were noted by the operating surgeons, but in the presence of the acute gallbladder pathology, they were interpreted as being inflammatory in origin.

These cases offer an interesting problem from a surgical point of view, for it is considered meddlesome surgery to carry out extensive abdominal exploration in the presence of an acute or suppurative lesion. It is, therefore, reasonable to assume that the underlying lesions were overlooked, first, because they were not suspected, and second, because the findings were those of an acute inflammatory process. One can merely suggest that when acute changes in the gallbladder are encountered, a careful search be made in the region of the common duct and head of the pancreas, providing that such exploration does not engender spread of the infectious process.

SUMMARY AND CONCLUSIONS

(1) Eight cases of acute cholecystitis occurring during the early course of neoplastic common bile duct obstruction are presented.

(2) In all cases, the gallbladder showed acute inflammation. In all cases, a malignancy which produced common duct obstruction was eventually discovered. The time interval between acute cholecystitis and symptoms referable to the malignancy varied from a few days to 12 weeks.

(3) In no case did the surgeon suspect a malignancy upon observing the acute cholecystitis at the operating table.

(4) The mechanism involved in the production of the acute exacerbation of the cholecystitis is discussed. The acute attack is attributed to the combined effects of circulatory changes and progressive common duct obstruction upon a gallbladder which is already diseased.

(5) Emphasis has been placed on the dangers of not recognizing the underlying neoplasm because of the existing acute inflammatory lesion.

We should like to express our appreciation to Dr. D. M. Grayzel for his assistance in assembling the pathologic material.

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STUDIES ON THE ABSORPTION OF SULFANILAMIDE FROM THE LARGE INTESTINE

RESULTS FOLLOWING THE ADMINISTRATION OF SUPPOSITORIES

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OUR recent experimental studies indicate that there is good absorption of sulfanilamide from the rectum as well as the colon.^{1, 2} In our studies on the absorption from the human large intestine,² warm (30° C.) 1 per cent solutions of sulfanilamide were employed. In normal individuals approximately 9 mg. of combined sulfanilamide per 100 cc. of blood were found following the rectal administration of 7 Gm. of the drug over a period of 24 hours. After about 19 Gm. of sulfanilamide had been given over a period of 72 hours, approximately 11 mg. of combined sulfanilamide per 100 cc. of blood were found.

In order to determine whether sulfanilamide is absorbed directly from the colon, or whether it passes into the ileum and is absorbed there, the same series of investigations were repeated in a subject who had no communication between the small intestine and the colon. A permanent ileostomy with exclusion had been performed in November, 1936, for a rapidly progressive chronic ulcerative colitis. Following operation, there had been an arrest of the disease except for the recurrent development of polypi. Although the colon in this case could not be considered normal, it afforded an excellent opportunity for the study of absorption of sulfanilamide from the large intestine. After the rectal administration of 14 Gm. of sulfanilamide over a period of about 65 hours, the blood showed a concentration of 15 mg. of combined sulfanilamide per 100 cc.

In order to investigate the absorption of the drug from the rectum, we utilized a subject who had had a resection of the sigmoid for a carcinoma. The proximal portion of the sigmoid had been brought out as a colostomy and the rectal stump had been closed and covered with peritoneum, after the method of Devine,³ leaving a defunctioning rectal pouch. After the administration of 18 Gm. of sulfanilamide in solution into the rectal pouch over a period of three days, the concentration in the blood was 11 mg. of combined sulfanilamide per 100 cc. This experiment definitely established the fact that sulfanilamide in solution is absorbed from the isolated rectum.

The following are the results of the studies on absorption of sulfanilamide

Submitted for publication June 1, 1939.

from the rectum and colon when given in suppository form. These studies were conducted under the same experimental conditions as described in our previous paper.² The blood concentrations were determined by the method of Marshall, as modified by Marshall and Litchfield.⁴

Protocol 1.—L. A., white, male, age 52, was admitted to the Brooklyn Hospital, December 4, 1938, with a diagnosis of fistula in ano. Examination was otherwise normal and he was considered suitable for this study. One gram of sulfanilamide incorporated in gelatin-glycerine suppositories was given at three-hour intervals for two doses. The concentration of the blood three hours after the first dose was 1 mg. free sulfanilamide per 100 cc. Three hours after the administration of the second dose, 2 mg. free sulfanilamide per 100 cc. of blood were found. This procedure was repeated the following day. Three hours after the administration of the first gram of sulfanilamide, the concentration of the blood was 1.5 mg. free sulfanilamide, and three hours after the administration of the second dose, it was 2.5 mg. free sulfanilamide per 100 cc. of blood.

We then studied absorption of sulfanilamide in suppository form, first from the colon and then from the rectum. In these experiments (Protocol 2A and 2B) we again employed the subject with the isolated rectal pouch.²

Protocol 2A.—Two suppositories, each containing 0.5 Gm. of sulfanilamide, were introduced into the rectal pouch every four hours, the midnight dose being omitted. After 5 Gm. of sulfanilamide had been given, a trace of the drug was noted in the blood; after 10 Gm. had been introduced, 1 mg. free and 1 mg. conjugated sulfanilamide were observed per 100 cc. of blood, and after a total of 15 Gm. had been given, 1.5 mg. free, and a trace of conjugated sulfanilamide were found per 100 cc. of blood. The investigation was terminated at this stage because of reasons unrelated to the experiment. Traces of sulfanilamide in the blood were observed about 30 hours after the last dose had been given.

Comment.—It is evident that sulfanilamide incorporated in suppositories is poorly absorbed from the isolated rectal pouch. The solution of sulfanilamide was absorbed well.² Thus, after the administration of 6 Gm. of 1 per cent solution of sulfanilamide over a period of 24 hours, 3 mg. free sulfanilamide per 100 cc. of blood was found; none of the conjugated form of sulfanilamide was present. After the administration of a total of 12 Gm. over 48 hours, the concentration of the blood was 3.5 mg. free and 1.5 mg. conjugated sulfanilamide per 100 cc. As already recorded, after a total of 18 Gm. of sulfanilamide had been given, 6 mg. free and 5 mg. conjugated sulfanilamide were observed per 100 cc. of blood.

Protocol 2B.—After preliminary determinations had shown no evidence of sulfanilamide, a study of absorption of sulfanilamide from the colon was begun. Two suppositories, each containing 0.5 Gm. of sulfanilamide, were introduced into the colostomy stoma every four hours, day and night. The patient was instructed to lie on his back for one hour after the insertion of the suppositories. In spite of this precaution, parts of the medication were expelled at times. After 6 Gm. of sulfanilamide had been given, 2 mg. of free sulfanilamide were found in each 100 cc. of blood; after the administration of 12 Gm., the concentration of the blood was 2.5 mg. free and 1.5 mg. conjugated sulfanilamide; and after a total of 18 Gm. of sulfanilamide had been administered, 3.5 mg. free and 1.5 mg. conjugated sulfanilamide were found per 100 cc. of

RECTAL ABSORPTION OF SULFANILAMIDE

blood. The concentration of the blood, 24 hours after cessation of therapy, was 1 mg. free and 1.5 mg. conjugated sulfanilamide per 100 cc.

Comment.—This experiment indicates that sulfanilamide in suppository form is absorbed better from the colon than from the rectum. Reliable comparative figures for absorption of sulfanilamide in solutions were not obtained owing to the fact that the solution was frequently expelled from the colostomy stoma.

Protocol 3A.—H. H., Negro, male, age 20, was admitted to the Brooklyn Hospital because of a left bubo and right inguinal lymphadenopathy. The Frei test, using three human antigens, gave strong positive reactions. A complete examination and laboratory tests disclosed that he was otherwise normal, and suitable for this study. Forty-eight hours after the bubo had been aspirated, a course of sulfanilamide therapy was instituted. One ounce of castor oil, followed by a colonic irrigation, was given one day before this study was begun. Two suppositories, each containing 0.5 Gm. of sulfanilamide, were administered every four hours, day and night. After the administration of 7 Gm. of sulfanilamide, the concentration of the blood was 1 mg. free and 1 mg. conjugated sulfanilamide per 100 cc.; after 13 Gm. had been given, the concentration of the blood was 2.5 mg. free per 100 cc.; none of the conjugated sulfanilamide was present (some of the medication was expelled on two occasions); after 19 Gm. of sulfanilamide had been given, 4 mg. free and 2 mg. conjugated sulfanilamide were found in each 100 cc. of blood; and after a total of 25 Gm. of sulfanilamide had been administered, the concentration of the blood was 6 mg. free and 2 mg. conjugated sulfanilamide per 100 cc. of blood. Blood, drawn 12 hours after cessation of therapy, and eight hours following a colonic irrigation, showed 3 mg. free sulfanilamide per 100 cc. Twenty-four hours later, 1 mg. free sulfanilamide was found. Traces of sulfanilamide were noted 48 hours after cessation of therapy.

Protocol 3B.—After preliminary determinations of the blood had shown no evidence of sulfanilamide, H. H. was given 100 cc. of a 1 per cent solution of sulfanilamide rectally every four hours, day and night. After 6 Gm. of sulfanilamide had been given, the concentration of the blood was 6 mg. free and 1 mg. conjugated sulfanilamide per 100 cc.; after 12 Gm. had been administered, 8 mg. free and 2 mg. conjugated sulfanilamide per 100 cc. were noted; after the administration of 18 Gm. of sulfanilamide, again, 8 mg. free and 2 mg. conjugated sulfanilamide per 100 cc. of blood were obtained; and after a total of 24 Gm. of the drug had been given, the concentration of the blood was 3.5 mg. free and 4 mg. conjugated sulfanilamide per 100 cc. Blood drawn 24 hours after cessation of therapy revealed 4 mg. free and 1.5 mg. conjugated sulfanilamide per 100 cc. After 48 hours, the concentration in the blood was 1.5 mg. free and 1 mg. conjugated sulfanilamide.

Comment.—Higher concentrations of sulfanilamide in the blood were noted in this experiment than in Protocol 3A, proving that greater absorption of sulfanilamide occurs when the drug is administered in solution than in suppository form.

Protocol 4.—E. W., white, female, age 28, had had chronic ulcerative colitis for four years. On March 11, 1939, she was sent to the Brooklyn Hospital with signs of hemoperitoneum. At operation, a ruptured corpus luteum in the left ovary with massive hemorrhage in the peritoneal cavity was found. After two blood transfusions of 500 cc. each, the hemoglobin value was 80 per cent (Sahli). On the twelfth postoperative day she was considered suitable for the study of absorption of sulfanilamide from the large intestine. Two suppositories, each containing 0.5 Gm. of sulfanilamide, were given every four hours, day and night. After the administration of 6 Gm. of sulfanilamide,

the concentration of the blood was 3 mg. free and 1 mg. conjugated sulfanilamide per 100 cc.; after the administration of 12 Gm., the concentration of the blood was 4 mg. free and 2 mg. conjugated; after 18 Gm. of sulfanilamide had been given, the concentration of the blood was 7 mg. free and 2 mg. conjugated; and after a total of 24 Gm. of sulfanilamide was given, the concentration of the blood was 6 mg. free and 1 mg. conjugated sulfanilamide per 100 cc. The blood concentration 24 hours after cessation of sulfanilamide therapy was 3.5 mg. free and 1.5 mg. conjugated sulfanilamide per 100 cc. After 48 hours, the concentration of the blood was 1 mg. free and 1.5 mg. conjugated sulfanilamide per 100 cc.

Comment.—Cyanosis and nausea were observed. This is the first instance of nausea seen in our studies of absorption of sulfanilamide from either the normal or diseased large bowel.

Proctosigmoidoscopic studies following the rectal administration of sulfanilamide showed no changes in the normal mucosa of the rectum or colon.

SUMMARY AND CONCLUSIONS

(1) Evidence is presented to show that sulfanilamide is absorbed from the rectum and colon when given either in solutions or in suppositories.

(2) Higher concentrations of sulfanilamide were noted in the blood, hence greater absorption, following the rectal administration of sulfanilamide in solution.

(3) The rectal route of administration of sulfanilamide is recommended whenever the oral route cannot be utilized. The same total dosage may be employed for the rectal as for the oral administration.

The sulfanilamide used in these experiments was supplied by the Medical Research Department, Winthrop Chemical Company.

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STRUMA LYMPHOMATOSA (HASHIMOTO)

REPORT OF TWO CASES

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THE FOLLOWING PATIENTS with "struma lymphomatosa" (Hashimoto) were seen at the Endocrine Clinics of the Evanston Hospital and Northwestern University. Operations were performed on the services of Doctors Koch and Mason at Passavant Memorial Hospital and Doctor Christopher at Evanston Hospital. One patient is a female in the third decade of life, and is of interest because of her age. The other, a male, almost in his seventieth year, is of extreme interest because nearly 100 per cent of reported, verified lesions occur in women.

The problem of so-called "chronic nonspecific thyroiditis" is still very confusing. Clinically, it seems to have little or no relation to definite previous acute inflammatory lesions. It seems best for the present to consider it of at least three types: Riedel's, or fibrous; Hashimoto's, or lymphoid; and a mixture of these two, or lesions which will fit neither of the above but still show evidence of a chronic process. Some authors doubt the existence of these as actual types and feel that they are but various stages in the same disease. It is not within the scope of this paper to enter this argument. However, we feel there are both clinical and histologic differences sufficient to separate Riedel's¹ and Hashimoto's² types. This is true if one will follow the original, definite descriptions of the lesions by the authors. The reader is referred to the excellent reports by Ewing,³ Graham,⁴ Graham and McCullaugh,⁵ Hertzler,⁶ Lee,⁷ McClintock and Wright,⁸ and Means⁹ for further discussion.

CASE REPORTS

Case 1.—M. B., female, age 28, married, was born in Wisconsin. She complained of nervousness, weakness, some palpitation and tachycardia, noticed mostly at night. She had had severe frontal headaches, two a day, for the past two months. The inventory by systems was essentially negative. She had jaundice when a child. There was no history of recent weight loss. Menarche at age 17. Menses are regular 28-day type with no pain and of five days' duration. There was one pregnancy with child, living and well, ten months old. No significant family history. The physical findings were: Blood pressure 116/70, pulse 80. The eyes were negative except that the right pupil appeared larger (?) than the left. There was a questionable tremor of the hands, and some dental caries. The heart, lungs, abdomen, and extremities were negative. The thyroid was palpable and firm. Laboratory studies showed: Whole blood cholesterol 163 mg.; basal metabolic rates: several were about plus 20, with pulse 96 to 88. Wassermann and Kahn, urine, *etc.*,

Submitted for publication April 26, 1939.

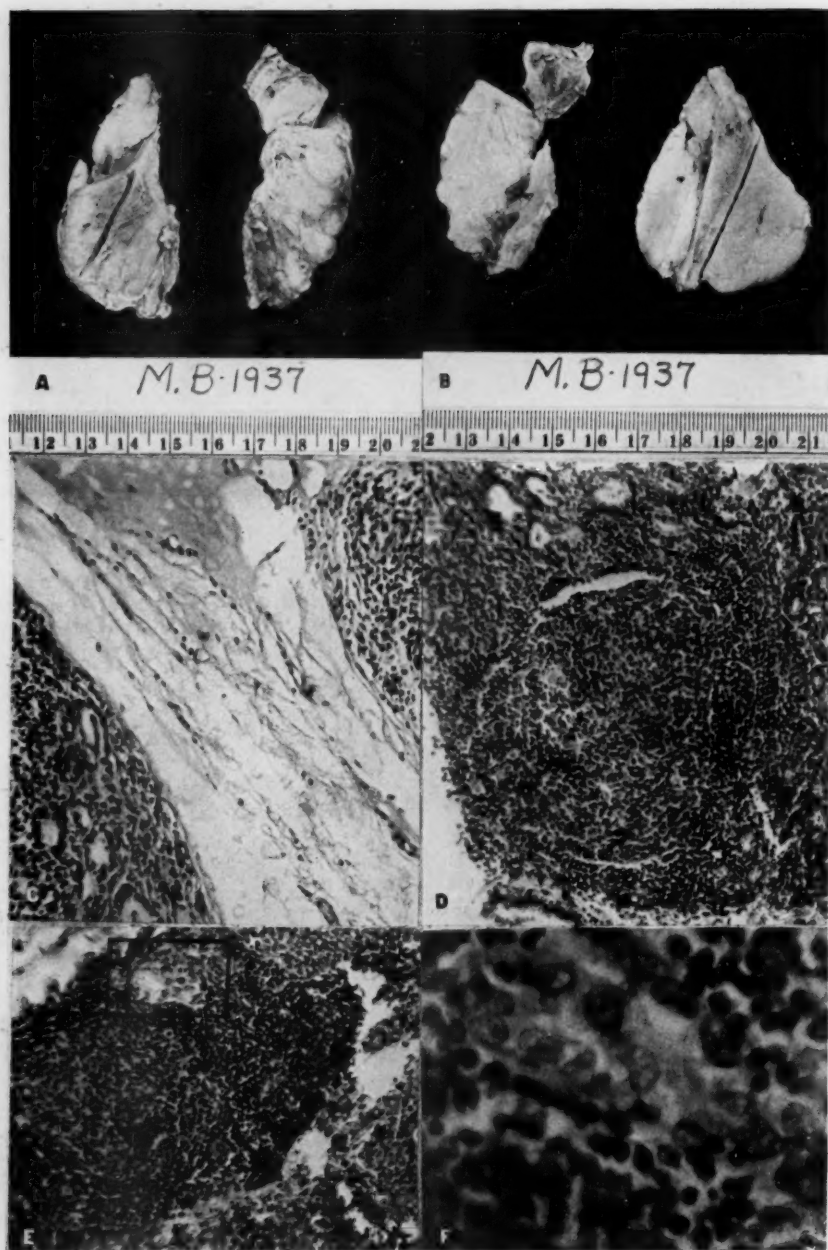


FIG. 1.—Struma Lymphomatosa Case 1.: A, Right and left lobes anterior surfaces, white and very hard; B, Cut sections of lobes showing grayish white surface; C, Connective tissue, $\times 80$; D, Lymph follicle with germinal center, $\times 80$; E, Lymph cell infiltration and acini with "foamy" cells, $\times 80$; F, High magnification of "foamy" cells in blocked area, $\times 500$.

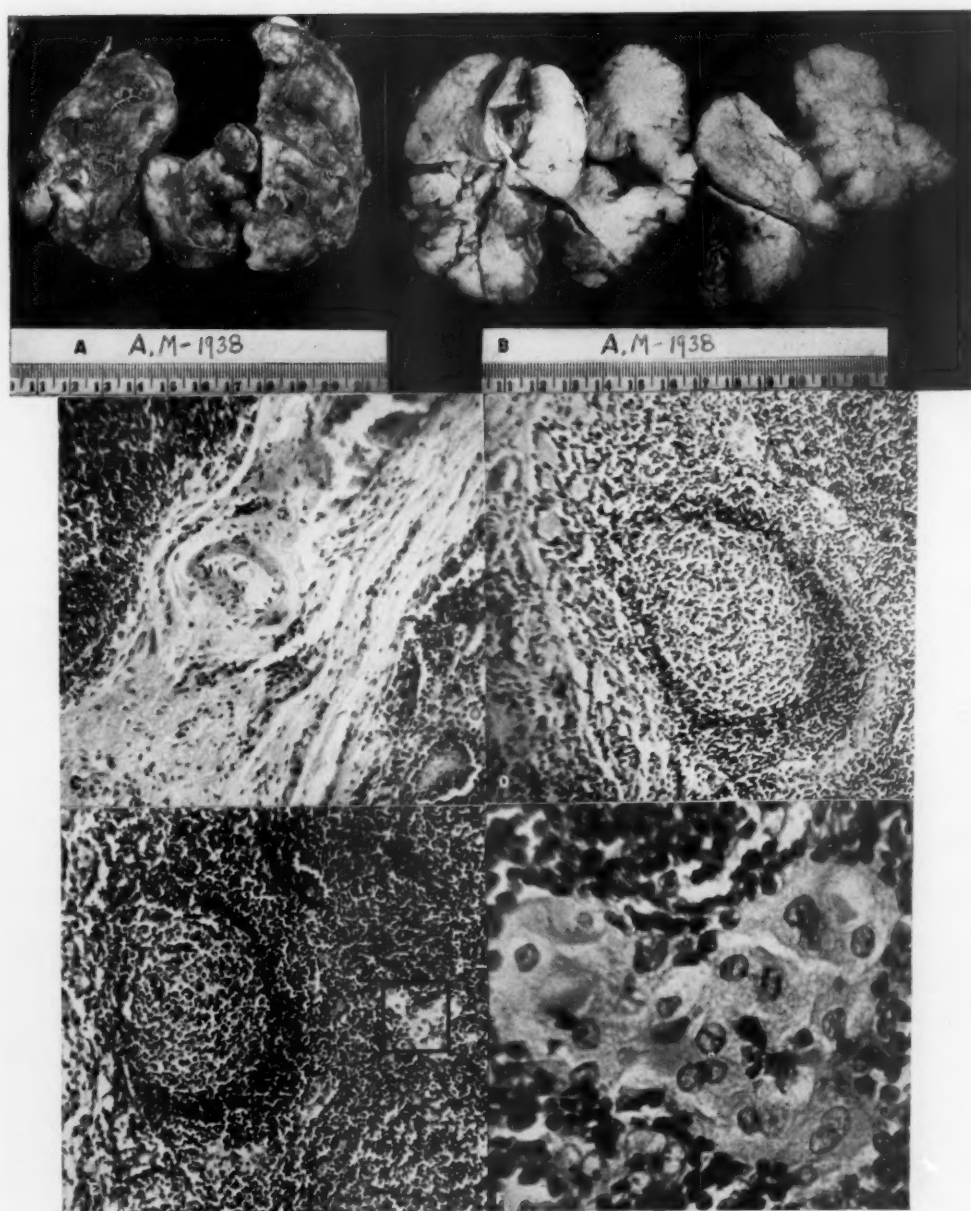


FIG. 2.—Struma Lymphomatosa Case 2.: A, Total thyroidectomy showing anterior surfaces of three lobes; B, Cut sections all lobes show mottled grayish white surfaces; C, Connective tissue, $\times 80$; D, Lymph follicle with germinal center, $\times 80$; E, Lymph cell infiltration and acini with "foamy" cells, $\times 80$; F, Higher magnification of "foamy" cells in blocked area, $\times 500$.

were negative. Blood counts were: Hemoglobin 72 per cent, red blood cells 4,280,000, white blood cells 5,700, and the electrocardiogram showed normal rate and rhythm. Roentgenologic examination of the chest was normal. The patient was hospitalized before operation and showed no response to Lugol's. At operation the gland was firm, fibrous and adherent. The weight of tissue removed was 24 Gm. (Fig. 2). She was discharged from the hospital on the ninth postoperative day. One year following operation, this patient is showing symptoms of hypometabolism, but still has a great deal of sympathicotonia.

Case 2.—A. M., male, age 65, a native of Persia. He complained of a mass in the neck with a feeling of tightness (past year), pain in back and shoulder (four months), loss of weight (12 lbs. in six years), more irritable and nervous (four months), pain in left leg (five years), difficulty on urinating (intermittently last four months), constipation (years), pain in chest (four to five years), dizziness (past year), cough (six months). Inventory by systems was essentially negative except as above. The physical examination showed: Pulse 68, respiration 20, blood pressure 144/84. There was a slight cyanotic tinge to the face with dilatation of veins over upper chest and neck. Dental caries present. The thyroid was enlarged bilaterally and firm. The heart, lungs, and extremities were negative. The abdomen was normal, except that the liver was slightly enlarged. The patient had no thyroid enlargement while living in Persia. He has been a resident of Chicago for 29 years and the goiter developed while here. The clinical impression was that in view of recent growth, symptoms, *etc.*, the thyroid should be removed immediately. Laboratory examination showed: Kahn negative, blood cholesterol 232 mg.; blood count, hemoglobin 80 per cent, red blood cells 4,740,000, white blood cells 8,850. The urine was negative. Several basal metabolic tests were between minus 10 and minus 15. Roentgenologic examination revealed no compression or displacement of the trachea. However, when barium was given by mouth it was seen fluoroscopically to pass, at all times, more to the right than to the left, as though there was some extrinsic mass causing pressure on the left side of the hypopharynx and upper esophagus. Examination of the neck showed slight constriction of the trachea at the point of entry into the thoracic cavity. Of interest are two "basal rates" taken after admission to the hospital. They were a plus 86 and plus 88 on different days and show the error possible with this test. Following operation there has been progressive hypothyroidism which was apparent before treatment and is being controlled with desiccated thyroid (Fig. 2).

In general, the pathologic examination of these two glands is similar. They are those of a hard gland with bilateral enlargement. The cut surface has a slightly granular, grayish-white appearance, mottled by darker areas and lobulated by bands of white connective tissue. The microscopic findings show intense infiltration of the interacinal spaces with lymphocytes and the presence of lymphoid follicles, many of them which have germinal centers. This infiltration may be so great that the acini are entirely obliterated. The acinal cells in some areas are large and appear "foamy." There is an absence of colloid. According to Hertzler,⁶ the "foamy" appearance and the clumping of the acinal cells are a constant feature of this lesion and are sufficient alone to distinguish it from the other types. There are areas of apparent hyperplasia in the glands, probably of a compensatory nature. The connective tissue is usually swollen, poorly stained, and the cells have few nuclei differing from that seen in the Riedel type which forms heavy keloid-like bundles.

Both specimens have been studied by Dr. Allen Graham of Cleveland, whose impressions in brief are as follows: In Case 1, the gland is suggestive of an "early" lesion similar to that described by Hashimoto, and in Case 2, the gland is typical for lesions described by Hashimoto.

SUMMARY.—Two patients with struma lymphomatosa (Hashimoto) are reported, one present in a male and the other in a young woman.

We wish to thank Doctors Koch, Mason and Christopher for the privilege extended in reporting these cases, and Dr. Allen Graham for his help and advice.

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BILATERAL AND BILOCULAR EMPYEMA

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RECENT OPPORTUNITIES to care for several patients with bilateral and bilocular empyemata have stimulated our interest in these complicated forms of thoracic empyema. In order to arrive at satisfactory conclusions regarding their incidence and treatment, we have reviewed the cases of empyema at the University of Michigan Hospital from January, 1925, until August, 1938. During this period, 418 patients suffering with thoracic empyema due to pyogenic organisms occurring following respiratory infections, were admitted to the various services of the hospital. These cases do not include those with pure or secondarily infected tuberculous empyema, those in which empyema followed thoracic operations such as pulmonary lobectomy, those secondary to esophageal perforation, those following spontaneous perforation of a pulmonary abscess into the pleural cavity, or contamination of the pleura subsequent to surgical drainage of a pulmonary abscess, and those secondary to subdiaphragmatic abscess.

Of the 418 patients, 187 were classified as having chronic empyema of from several weeks' to years' duration at the time of admission. Many of these patients had had surgical or medical care elsewhere; their management at the University Hospital ranged from simple dilatation of a contracted drainage track to an extensive Schede thoracoplasty. The operative mortality rate in this group was 1.16 per cent, only two patients having died while in the hospital.

During the years covered by this study, several methods of treatment were employed in the care of the 231 patients having acute empyema. All have been based, however, upon the well-understood principles of avoiding the establishment of an open pneumothorax until the lung has become fixed by pleural adhesions and of instituting early dependent drainage. Thirty-one of these patients died, giving a mortality rate of 12.4 per cent.

BILATERAL EMPYEMA

In Table I are presented the 12 cases of bilateral empyema occurring during the period of the study, an incidence of 2.9 per cent. Of these, three (Cases 2, 6 and 12) may be classified as chronic, while nine were acute at the time of admission. Four patients did not receive treatment, empyema not

Submitted for publication May 24, 1939.

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TABLE I
BILATERAL EMPYEMA

No.	Patient	Age	Sex	Interval from Onset to Adm.	Etiologic Organism	Treatment	Remarks
1	C. V.	34	M.	3 days	Unknown	None	Developed lobular pneumonia 10 days following herniorrhaphy. Died 3 days later. Autopsy: Rt. empyema, 1,100 cc.; lt., 700 cc. Neglected case of chronic empyema admitted in bad general condition. Died 4 days later, in spite of transfusion and efforts to improve nutrition.
2	M. S.	18 mos.	M.	4 mos.	Unknown	Aspiration for 2 days. Rt., open drainage; lt., closed drainage—at one operation	Admitted gravely ill. Death in 2 days. Autopsy: Bilateral lobular pneumonia; rt. empyema, 300 cc.; lt., 750 cc. Premature infant dying of lobular pneumonia. Autopsy: 20 cc. of pus in each pleural cavity
3	C. L.	14	M.	2 days	<i>Streptococcus viridans</i> (blood culture)	None	Aspiration of lt. empyema continued after drainage of right. Rt., closed drainage unsatisfactory. Cured
4	R. H.	2 mos.	M.	Developed in hospital	Unknown	None	
5	294590 M. C.	17	M.	2 wks.	Rt., Type I pneumococcus. Lt., Type I pneumococcus	Bilateral aspiration for 10 days. Rt., closed intercostal drainage followed by open in 2 days; lt., open drainage 3 wks. later	
6	W. S.	6	M.	3 mos.	Rt., hemolytic <i>Streptococcus</i> . Lt., unknown	Rt., open drainage; lt., operative closure of bronchopleural fistulae	Lt. empyema had closed intercostal drainage elsewhere. Admitted with rt. empyema and lt. pneumothorax, with bronchopleural fistulae. Lt., operation after healing of rt. empyema. Cured
7	J. S.	6	F.	Onset. Admitted with pneumonia	Rt., Type II pneumococcus. Lt., unknown	Bilateral aspiration. Rt., open drainage after 10 days' aspiration	Diagnosed at onset. Rt. empyema more severe. Bronchopleural fistula and 2 pockets present on rt. (see Table II). Child
8	E. Z.	13	F.	1 day	Rt., <i>Streptococcus viridans</i>	Rt., repeated aspiration; lt., repeated aspiration	Admitted with rt. empyema. Lt. developed 8 days after admission, with rt. already cured. Cured
9	344352 J. W.	9	M.	Onset. Admitted with peritonitis from ruptured appendix	Rt., <i>Streptococcus viridans</i> . Lt., <i>Streptococcus viridans</i> and <i>haemolyticus</i>	Rt., aspiration for 2 mos.; lt., open drainage after 4 wks. aspiration. Daily bilateral aspirations for 3 wks.	Empyema on rt. developed and aspirated 6 days after admission and just before appendectomy and drainage. Had had previous conservative therapy for peritonitis. Lt. empyema developed 1 wk. after rt. Child gravely ill. Cured
10	A. G.	18	M.	Onset in hospital	Type IV pneumococcus (sputum)	None	Admitted with bilateral pneumonia. Died after 20-day illness. Autopsy: Bilateral bronchiectasis, bronchiectatic abscesses, unresolved pneumonia; rt. empyema, 1,500 cc.; lt. empyema, 500 cc.
11	R. B.	5	M.	3 days	Rt., Type V pneumococcus. Lt., unknown	Bilateral aspiration, 4 wks. Rt., open drainage; lt., continued aspiration for 3 wks.	Daily bilateral aspiration for 2 wks. Cured
12	R. L.	35	M.	2 mos.	Rt., Type I pneumococcus. Lt., Type I pneumococcus	Rt., open drainage; lt., open drainage	Lt., bronchopleural fistula. Lt., therefore, drained first, and rt. 2 days later

having been diagnosed until postmortem examination; Cases 1 and 3 died after brief illnesses with bilateral lobular pneumonia; Case 4 is that of a premature infant dying of malnutrition and pneumonia, with very small amounts of pus in both pleural cavities; Case 10 was admitted with a tentative diagnosis of bilateral lobular pneumonia and was apparently recovering until a sudden change in his condition occurred two days before his death; the postmortem examination demonstrated bronchiectasis, bronchiectatic abscesses, and bilateral empyema.

Of the eight treated patients with bilateral empyema, one was cured by bilateral aspiration. Three patients were treated with aspiration alone on one side and with open drainage, following aspiration, on the contralateral side. Aspiration followed by bilateral drainage was employed for one patient, three weeks intervening between the drainage operations. Prolonged aspiration was deemed unnecessary for Case 12 in view of its chronic nature; the two sides were drained two days apart following diagnostic taps. The one patient who died was an 18 month old child, admitted with bilateral empyemata of four months' duration, and in extremely poor general condition. Following aspiration for two days, in order to diminish the amount of thick pus in the hemithoraces, both sides were drained by an efficient air-tight technic at one operation; the child died four days later of advanced malnutrition in spite of transfusions and other efforts to improve his condition. Case 6 presented an interesting condition; on admission, a right-sided empyema was present, while on the left side there was an apparently uninfected pneumothorax with multiple bronchopleural fistulae, which had developed following drainage of a left-sided empyema elsewhere; the drainage tract was healed. Cure of the right-sided empyema followed drainage; after complete healing of the right-sided empyema a left thoracotomy was performed with suture of the fistulae and air-tight closure of the thoracic wall without drainage; the left lung slowly reexpanded and complete recovery ensued.

The operative mortality in the eight treated cases was 12.5 per cent. This is a lower percentage than we have been able to find in any other group comprising more than one or two cases reported in the literature, with one exception. The mortality rate of treated bilateral empyema is almost exactly that of the entire group of acute empyema cases in the University Hospital. In reviewing the methods of treatment employed in our cases, it is noticeable that for acute empyemata aspiration was persisted in for a much longer period than the average time. Furthermore, of the 16 empyemata in eight patients, five were cured by aspiration alone; this is a proportionately greater number than in the unilateral group. In no case, it should be noted, did cardiac or respiratory symptoms follow open drainage with the institution of efficient air-tight drainage.

ILLUSTRATIVE CASE REPORT

Case Report.—Bilateral Empyema: R. L. (Case 12, Table I; Figs. 1 to 4), male, age 33, was admitted to the University Hospital, July 8, 1938. Eight weeks previously he

BILATERAL AND BILOCULAR EMPYEMA

had developed bilateral empyema secondary to lobular pneumonia; his physician had performed numerous thoracenteses. After four weeks, persistent cough became productive of large amounts of purulent sputum. On admission, the patient was febrile and quite debilitated; his sputum was purulent and moderate in amount. Physical examination and roentgenologic studies demonstrated pleural effusions in both hemithoraces posteriorly; the presence of a definite fluid level on the left side, and the purulent sputum suggested the presence of a bronchopleural fistula. Bilateral thoracenteses demonstrated pus, in which cocci were found on smear, and from which Type I pneumococci were cultured.

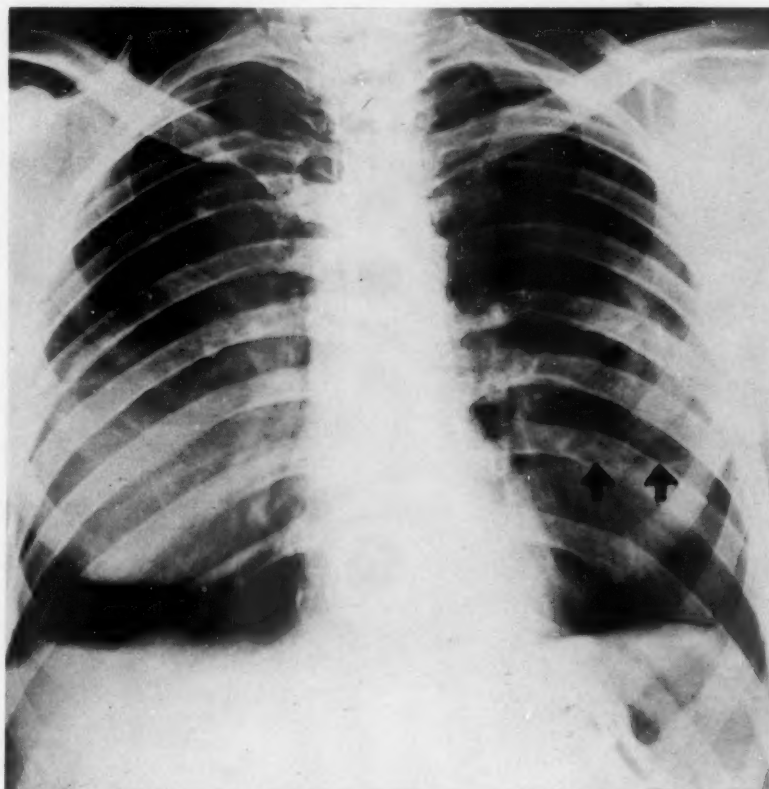


FIG. 1.—Case 12, Table I: Postero-anterior roentgenogram demonstrating bilateral pleural effusion with fluid level on left side.

Because of the probable left-sided bronchopleural fistula, the left empyema was drained first on the day of admission. Closed, dependent drainage was instituted following the resection of a portion of the eighth rib in the midscapular line, under local anesthesia. On July 10, two days later, the empyema on the right side was dependently drained, with the resection of a portion of the ninth rib in the midscapular line; closed drainage was established. Since both tubes had necessarily been placed in the posterior portion of the chest, drainage was cut off by the patient lying on his back. Closed drainage was, therefore, abandoned, and the tubes were cut off just external to the skin. This was safe in view of the chronicity of the empyemata and the probable fixation of the lungs and mediastinum. The patient made an uneventful recovery with complete obliteration of the empyemata.

In 1903, Hellin¹ collected the reports of 114 cases of bilateral empyema. The mortality rate was 30.1 per cent, which he considered too low to be representative in view of the tendency to communicate only with successfully treated single and series of cases. He estimated that bilateral pleural involvement occurs in 7.7 per cent of all empyemata. Keyes² found 38 cases in the

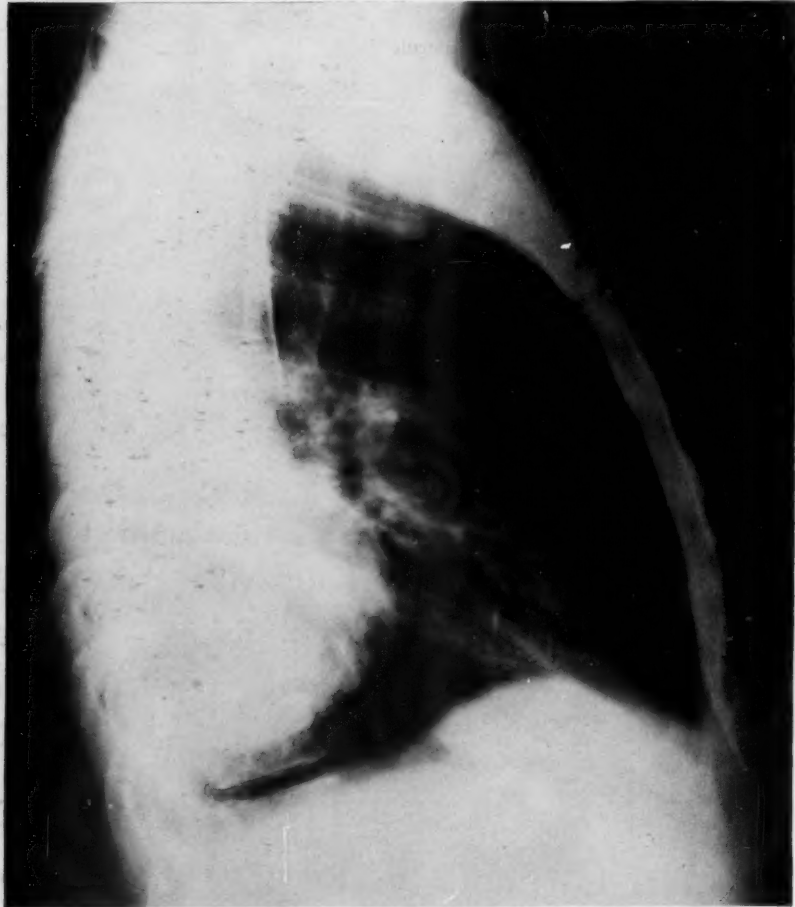


FIG. 2.—Case 12, Table I: Right lateral roentgenogram demonstrating that both empyemata lie posteriorly. The left empyema, with fluid level, is obscured by the right.

literature from 1910 to 1930, and added three treated at the New York Hospital. During the exceptionally grave influenza epidemics of 1917-1918, Stevens³ noted that 29.64 per cent of patients with bilateral pneumonia also suffered with empyema; in 40 per cent the pleural disease was unilateral and in 60 per cent bilateral. Unilateral *Streptococcus* empyema resulted in a mortality rate of 42.2 per cent and bilateral of 89.1 per cent; bilateral pneumococcus lobar pneumonia resulted in a mortality rate of 21.6 per cent when associated with unilateral empyema, and of 78.3 per cent with bilateral empyema; the

bilateral *Staphylococcus pneumonia-empyema* was almost invariably fatal. Dunham⁴ reported 536 autopsies of patients dying of empyema during the 1917-1918 epidemics; of this group, 245, or 45.7 per cent, had bilateral empyema. Maes, Veal and McFetridge⁵ found, however, only one instance of

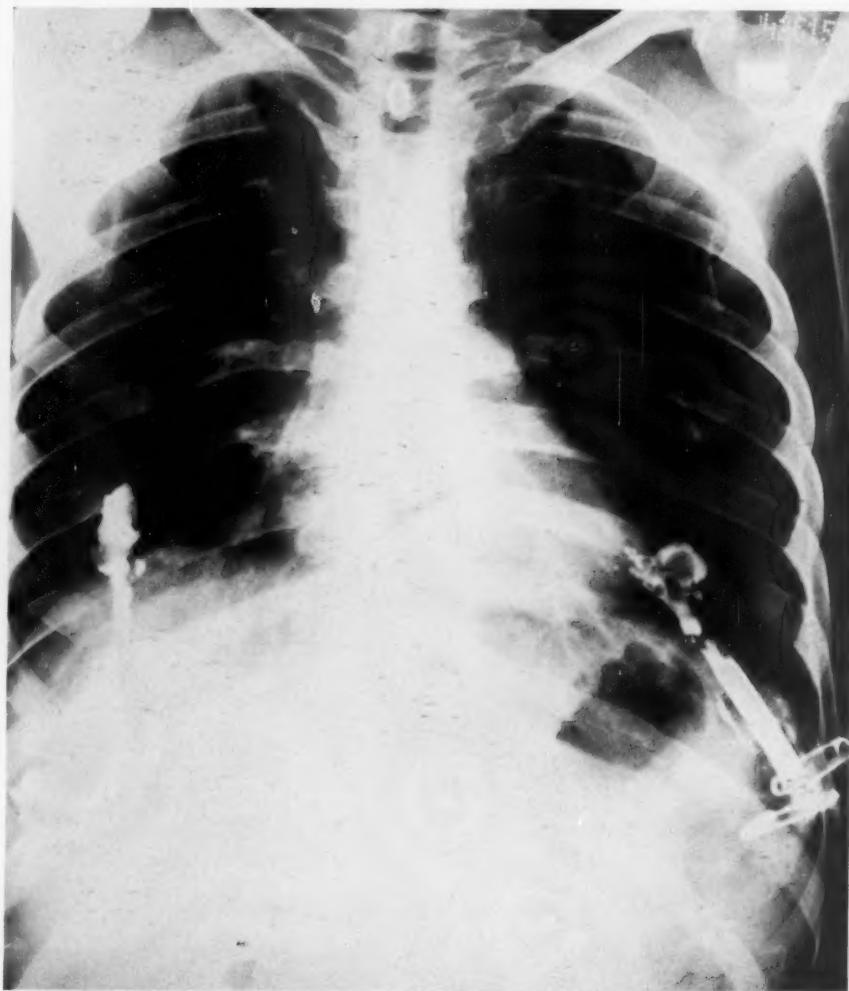


FIG. 3.—Case 12, Table I: Postero-anterior roentgenogram taken 31 days following drainage of the empyema on the left side, and 29 days after the drainage of that on the right side; iodized oil has been injected into the sinuses.

bilateral involvement among 100 fatal cases of empyema at the Charity Hospital of Louisiana.

We have endeavored to determine the incidence of bilateral empyema by gathering statistics from a number of articles on empyema published since 1921. Reports of single or several isolated cases have been disregarded since they do not furnish reliable information with regard to incidence.

The articles by Ladd and Cutler,⁶ Brown,⁷ Farr and Levine,⁸ Ravnitsky and Bogin,⁹ Ochsner and Gage,¹⁰ Keyes,² Locke,¹¹ Bauer,¹² Cohen,¹³ Rentschler,¹⁴ Steinke,¹⁵ Harloe,¹⁶ Bohrer,¹⁷ Michalowicz,¹⁸ Steinke,¹⁹ Burpee,²⁰ Utter,²¹ and Schmidt²² report 5,664 cases of empyema, of which 101 were bilateral, an incidence of 1.8 per cent. The articles by Beye,²³ Peck and Cave,²⁴ Rienhoff and Davison,²⁵ Foster,²⁶ Hudson,²⁷ Muller,²⁸ Jamin,²⁹ Danna,³⁰ Graham and Berck,³¹ Brann,³² Kalges,³³ McEachern,³⁴ Carlson and

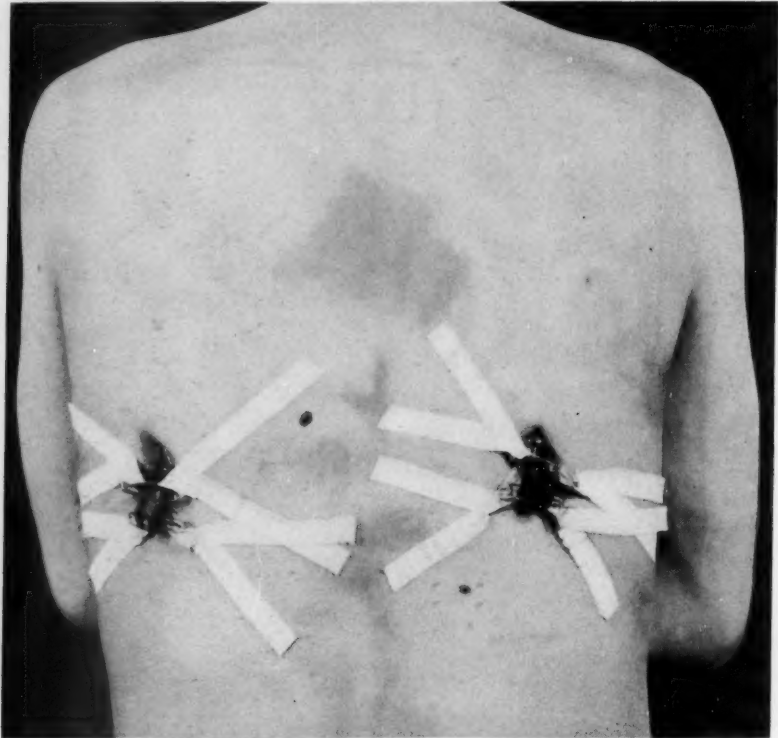


FIG. 4.—Case 12, Table I: Photograph of the patient showing the drainage sites.

Bowers,³⁵ Tanner,³⁶ Mason,³⁷ Penberthy and Benson,³⁸ and Niemeier³⁹ list an additional 2,155 cases in series not containing any bilateral case. The incidence of bilateral empyema in the entire group of 7,819 cases is 1.3 per cent.

The results of treatment in the large groups of patients with bilateral empyema are interesting. Ochsner and Gage¹⁰ reported five cases without a death, but did not mention the exact mode of treatment. Seven of Locke's¹¹ 11 patients with bilateral empyema died, two of Harloe's¹⁶ eight, one of Bohrer's¹⁷ six, 25 of Michalowicz's¹⁸ 28, and all of Steinke's¹⁹ 11. Aside from the results of Ochsner and Gage,¹⁰ the best results published prior to our series are those of Bohrer,¹⁷ with a mortality rate of 17 per cent, and of Harloe,¹⁶ with 25 per cent. These authors treated their bilateral cases with closed intercostal drainage. Bohrer¹⁷ performed the bilateral operations one

BILATERAL AND BILOCULAR EMPYEMA

or two days apart, while Harloe¹⁶ drained both sides at the same operation; similar drainage was used for their unilateral cases.

BILOCULAR EMPYEMA

Among the 418 patients with empyema were 13 with bilocular pockets in the same pleural cavity, giving an incidence of 3.1 per cent. Of the 13 cases, one was admitted following drainage elsewhere, one developed in the hospital, one was of three weeks' duration on admission, one of one month's,

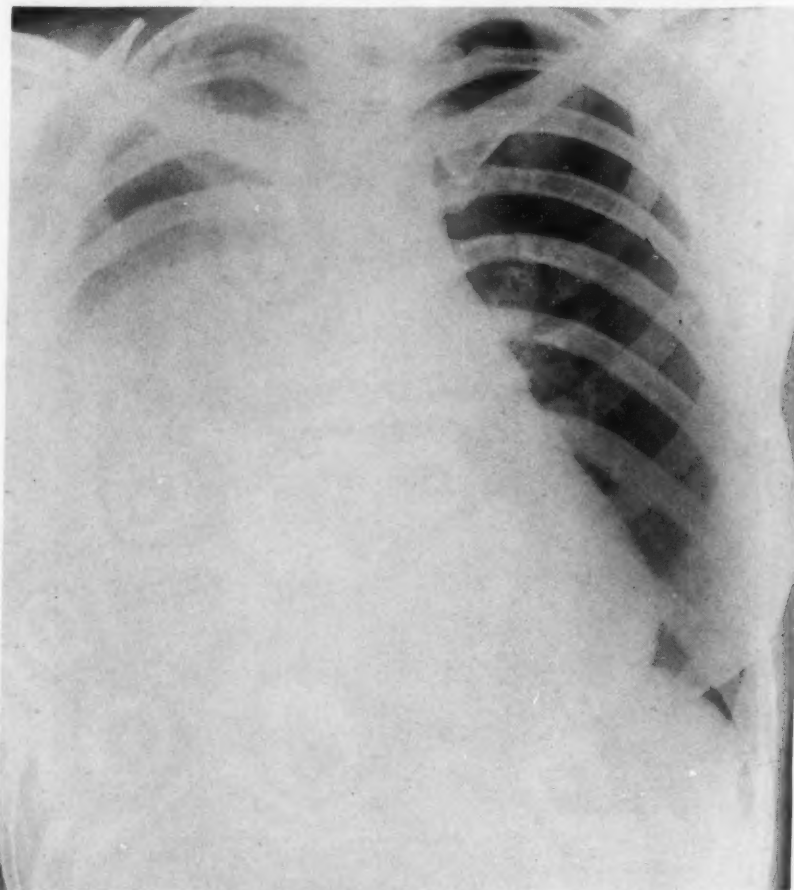


FIG. 5.—Case 12, Table II: Postero-anterior roentgenogram, taken on admission to hospital, demonstrating the right pleural effusion.

three of six weeks', five of four months', and one of 14 months'; it should be noted that only three may be considered early cases. In two cases (Cases 3 and 11), the pockets were widely separated at the base and apex, and the diagnosis was made preoperatively. In Case 9, which was admitted with a draining wound, the diagnosis of an undrained pocket was apparent before the second operation. In three cases (Cases 4, 5 and 6), the bilocular condi-

tion was discovered at the time of operation, when both pockets were drained, in Case 6, previous closed intercostal drainage had been instituted one month prior to open operation, with rib resection. In the remaining seven cases, the diagnosis of a second, undrained pocket was made from five days to three months following initial operation. In only five cases, including the three in which the diagnosis was made during the course of operation, was it possible

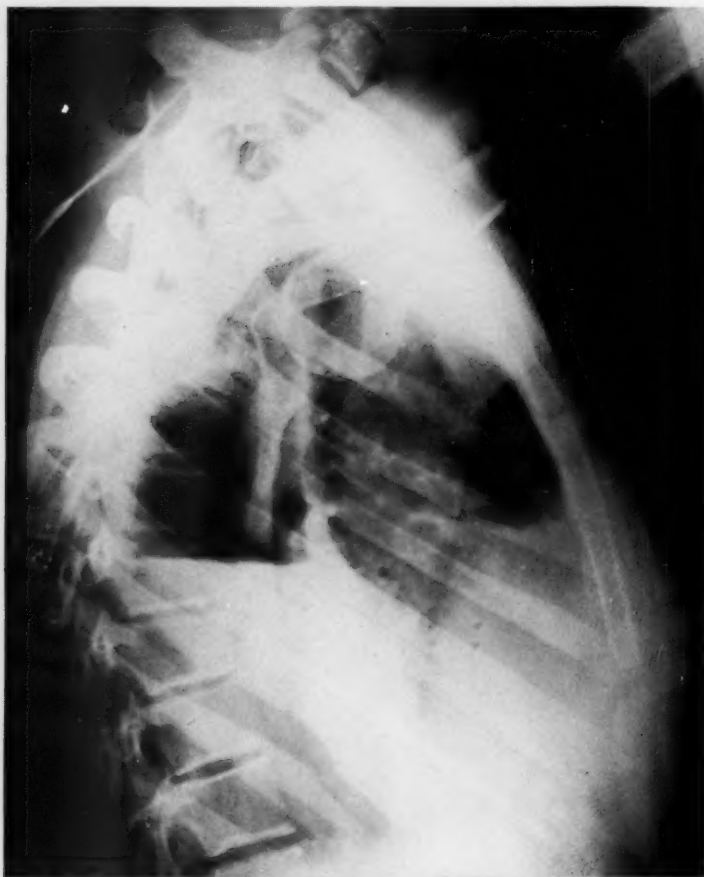


FIG. 6.—Case 12, Table II: Right lateral roentgenogram taken following aspiration of pus and injection of air before transfer to the Thoracic Service. Anterior and posterior fluid levels are clearly visible.

to institute double drainage through a single operative wound; in the remaining eight cases two incisions were needed.

Only two patients died. The cause of death in Case 9 was multiple actinomycotic liver abscesses, the patient dying after closure of the empyema, which was probably caused by the same organism. Case 6 died of osteomyelitis of the ilium, which developed while his empyema was draining, the osteomyelitis probably being metastatic; it is possible that earlier recognition and drainage of the second empyema pocket might have effected an earlier

BILATERAL AND BILOCULAR EMPYEMA

TABLE II
BILOCULAR EMPYEMA

No.	Patient	Age	Sex	Dura- tion	Etiologic Organism	Means of Diagnosis	Treatment	Remarks
1	C. E. 239773	5	M.	3 mos.	Type II pneumococcus	Postoperative x-ray	Drainage of second pocket through first incision, 5 days later	Continued fever led to study. Cured
2	E. K. 307012	7	F.	6 wks.	Type I pneumococcus and <i>Streptococcus</i>	Postoperative x-ray	Separate drainage of 2 pockets. 1-mo. interval	Diagnosis of bilocular empyema suspected on admis- sion. Symptoms recurred after first drainage. Cured
3	F. S. 334462	20	M.	4 mos.	Type I pneumococcus and <i>Streptococcus haemolyticus</i>	Preoperative x-ray	Separate drainage of 2 pockets with 2 separate incisions. 4- day interval	Superior and inferior pockets well separated. Cured
4	T. O. 336130	30	F.	6 wks.	Type I pneumococcus	At operation	Both drained through one inci- sion	Cured
5	J. S. 341343	6	F.	Onset	Type II pneumococcus	At operation	Second pocket opened at opera- tion through same wound	Bilateral empyema (see Table I). Biloculation sus- pected by x-ray. Bronchopleural fistula closed later by plastic operation. Cured
6	R. H. 343608	20	M.	4 mos.	<i>Streptococcus nonhaemolyticus</i>	At operation	At open drainage, 1 mo. after closed intercostal drainage, sec- ond pocket found and drained. Later re drainage necessary	Empyema cured. In meantime, developed a metastatic osteomyelitis of ilium causing death 1 yr. after first admission
7	A. J. 375500	5	F.	1 mo.	Type I pneumococcus	Postoperative x-ray	Separate drainage of 2 pockets. 7-wk. interval	Second pocket required re drainage. Lay superiorly. Cured
8	F. S. 384330	4	M.	6 wks.	<i>Streptococcus nonhaemolyticus</i>	Postoperative x-ray	Separate drainage of 2 pockets. 6-wk. interval	Persistent recurrent symptoms led to study. Cured
9	C. N. 388287	53	M.	3 mos.	No growth on cultures. <i>Actinomyces?</i>	Preoperative x-ray	Admitted with drained empy- ema and large undrained ante- rior pocket. Drained through old wound	Died 5 mos. later of multiple actinomycotic liver ab- scesses that had been in part drained
10	D. L. 410550	17	F.	4 mos.	(1) <i>Streptococcus haemolyticus</i> , (2) As above with <i>B. coli</i>	Postoperative x-ray	Separate drainage of 2 pockets. 4-wk. interval	Persistent symptoms. Second pocket anterior. Schede thoracoplasty later for posterior pocket. Cured
11	L. C. 411210	52	F.	4 mos.	Type III pneumococcus in both	Preoperative x-ray	Separate drainage of 2 pockets. 2-day interval	Widely separated anterior-superior and posterior-infe- rior pockets. Cured
12	E. K. 415444	16	F.	3 wks.	Type V pneumococcus	Postoperative x-ray	Separate drainage of 2 pockets. 8-day interval	Persistent symptoms followed first drainage. Cured
13	W. B. 416205	27	M.	4 mos.	(1) Anaerobic <i>Streptococcus</i> <i>haemolyticus</i> , (2) <i>Strepto-</i> <i>coccus viridans</i>	Aspiration	Separate drainage of 2 pockets. 3-mo. interval	Returned to hospital after closure of first pocket. Re- current symptoms found due to small lateral pocket, originally interpreted in roentgenogram as thickened pleura. Cured

cure of the empyema and prevented the metastatic infection. The mortality rate for the series of 13 cases of bilocular empyema is 15 per cent; if the patient who died of hepatic actinomycosis is eliminated, the rate is 8.3 per cent.

The only instance of an empyema with more than two separate pockets treated at the University Hospital occurred in a male, age 23, who was ad-

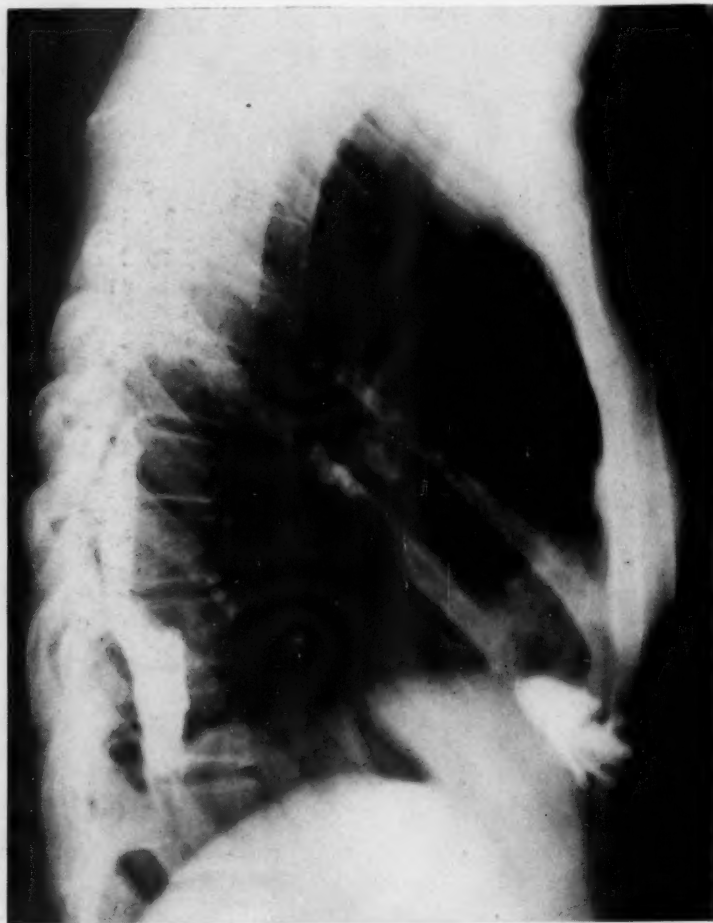


FIG. 7.—Case 12, Table II: Right lateral roentgenogram taken 45 days following drainage of the posterior pocket, and 37 days following the anterior; iodized oil has been injected into the sinuses.

mitted with a subphrenic abscess which was later drained. Three distinct empyema pockets were drained, as recognized, with separate rib resections, before the patient was discharged, apparently well. Various organisms of the pyogenic group were cultured, as well as *Actinomyces*.

ILLUSTRATIVE CASE REPORT

Case Report.—Bilocular Empyema: E. K. (Case 12, Table II; Figs. 5 to 8), female, age 16, was admitted, January 4, 1938. A diagnosis of postpneumonic empyema had been

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made ten days previously. Physical examination and roentgenologic studies demonstrated a large effusion in the right chest. Daily thoracenteses were performed for five days, with replacement of air on several occasions; Type V pneumococcus was cultured from the aspirated pus.

After transfer to the Section of Thoracic Surgery on January 10, a portion of the tenth rib was resected with the institution of closed air-tight drainage. The surgeon believed that all the empyema pus had been drained. The patient's temperature remained elevated, however, and a comparison of the preoperative and postoperative roentgenograms disclosed an anterior undrained pocket, which was especially well demonstrated in the lateral view. On January 18, a segment of the fifth rib was removed through a submammary incision with the removal of 180 cc. of pus from the pocket; closed drainage was employed. Both pockets became completely obliterated.



FIG. 8.—Case 12, Table II: Photograph of the patient showing the drainage sites.

Van Allen⁴⁰ treated one patient with three empyema pockets in one pleural cavity, which arose, he believed, from separate bronchopneumonic foci; they were drained by separate incisions made as each pocket was discovered during a 15-day period. Lilienthal⁴¹ drained five separate pockets at one operation; three distinct organisms were cultured. Mason³⁷ reported the drainage of three pockets through two incisions. Of 351 cases of acute empyema reported by Harloe,¹⁶ 2.27 per cent were multilocular. Danna,³⁰ in treating 75 cases of acute empyema with aspiration and air replacement, found three with multiple loculations, one of which had three pockets in the same pleural cavity.

SUMMARY AND CONCLUSIONS

In a large collected group of empyema cases, the incidence of bilateral empyema was 1.3 per cent; in our own series of 418 cases, it was 2.9 per cent. The operative mortality in eight treated cases was 12.5 per cent, which is almost identical with that of acute empyema in the same hospital. The good

results obtained from treatment resulted, we believe, from the meticulous care taken in these cases to observe the proper principles of therapy.

Loculation of pus in two places in the same pleural cavity occurred in 13 of our patients, an incidence of 3.1 per cent. Loculation occurred chiefly in chronic empyema. Recognition of multiple loculation depends upon careful study of preoperative and postoperative postero-anterior and lateral or oblique roentgenograms whenever the condition is suspected from clinical and physical findings. The foci should be drained as they are recognized, either through the original or supplementary incisions.

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THE TREATMENT OF PERIANAL TUBERCULOSIS

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SIXTY YEARS AGO, regarding operation in this condition, Allingham¹ wrote: "I should say from my experience, if you have a phthisical patient suffering from a fistula which gives him much pain or inconvenience, by taking certain precautions you may relieve him of it without running any risk of damaging him." In recent years excellent results have been reported following radical excision of perianal infections in patients with active pulmonary tuberculosis. Martin,² at the Chicago Municipal Sanatorium, reported 87 per cent cures in 75 cases; Berry,³ at Bellevue Hospital, had 72 per cent cures in 18 cases; and Chisholm,⁴ in Denver, cured 98 per cent of 71 patients.

Unfortunately, however, the erroneous and outmoded concept that perianal tuberculous infections should be treated conservatively has survived. The belief is widely held that these conditions in patients with pulmonary tuberculosis, when operated upon, are apt to recur; that the lung disease may be reactivated or made worse. This conservative attitude is deeply entrenched in the minds of internists as shown by answers of 28 Colorado phthisiologists to a questionnaire as to operative treatment of perianal infections in tuberculous patients (Table I).

TABLE I

PERIANAL INFECTIONS IN PATIENTS WITH PULMONARY TUBERCULOSIS

All More Than 70 Per Cent Positive Biopsy for Tuberculosis

Name of Author	No. of Cases	Cures
Martin ² (Chicago).....	75	71 (87%)
Berry ³ (Bellevue, N. Y.).....	18	14 (72%)
Chisholm ⁴ (Denver).....	71	70 (98%)

DO YOU RECOMMEND OPERATION?

Chisholm's⁴ Questionnaire to 28 Colorado Physicians

Yes.....	2
No.....	22
Selected Cases.....	4

My interest in this problem was stimulated some years ago by the apparent disinterest in the management of perianal infections occurring in tuberculous patients in one of our large municipal hospitals. Surgery consisted in conservatively incising abscesses and merely opening fistulae, with the result that few patients were cured or definitely improved. Patients with wide-

Submitted for publication May 16, 1939.

PERIANAL TUBERCULOSIS

spread perianal abscesses and multiple fistulae were considered inoperable, with the result that they continued a miserable existence, many of them veritably lying in a bed of tuberculous pus. Noxious effects resulting from the presence of pus in these patients were manifested by systemic reactions such as fever, anorexia, weight loss and amyloidosis. Pain depended upon the severity of the inflammatory reaction and anatomic distribution of the lesions.

The despondence of these patients was graphically described by Allingham¹ as follows: "There is a circumstance which occasions me sometimes to interfere in a case of fistula in phthisical patients, and that is, the mental depression which the rectal affection creates. Frequently the sufferer thinks much more about his fistula than he does about what he calls 'his little cough,' and is quite dismayed and brought to despair when you tell him that you cannot do anything to cure him. I am certain that few things conduce more to the rapid progress of phthisis than mental anxiety and loss of hope."

A Proctologic Service was instituted at the Sea View Hospital for Tuberculosis in 1935, primarily to study methods of management of these extensive perianal tuberculous lesions. Table II demonstrates that many active perianal infections were present in patients at Sea View, and that individuals so afflicted readily accept surgery when offered a chance for cure.

TABLE II

OPERATIONS FOR PERIANAL INFECTIONS AT SEA VIEW HOSPITAL

Abscesses, Fistulae or Both

1928 through 1931.....	1
1932 through 1934.....	14

Proctological Service Instituted April, 1935

1935.....	14
1936.....	23
1937.....	25
1938.....	29

Perianal infections are frequent in patients with pulmonary tuberculosis. Walsh reported perianal abscesses or fistulae found at autopsy in 9 per cent of a series of patients dead of phthisis. Frequency of perianal infections complicating pulmonary tuberculosis varied from 5 per cent, reported by Chisholm, of Denver, to 11.7 per cent reported by Marino,⁵ of Brooklyn, in a carefully studied group of 357 tuberculous patients at the Kingston Avenue Hospital.

In the general nontuberculous population, anorectal infections occur in 0.5 to 0.6 per cent (Table III). From these statistics, it is reasonable to conclude that tuberculous perianal lesions probably originate, in most instances, through contact infection with tubercle bacilli in the stools of phthisic patients. The mechanism of infection, I believe, depends on the clinical type

of perianal lesion present. Commonly seen are: Perianal abscess: (A) discrete—circumscribed; (B) serpiginous—subcutaneous. Fistula or sinus. Tuberculous anal fissure or ulcer. Lupus of the anus. Tuberculid.

TABLE III
INCIDENCE OF CHRONIC PERIANAL INFECTION

<i>Sinuses, Fistulae, Abscesses</i>		
Pulmonary Tuberculosis Hospitals		
Martin, ²	Chicago Municipal Sanatorium.....	7.0 %
Chisholm, ⁴	Denver, Jewish National San.	5.0 %
Marino, ⁵	Brooklyn, Kingston Avenue.....	11.7 %
General Hospitals		
Leslie, ⁹	Vancouver General Hospital.....	0.52 %
Leslie, ⁹	Massachusetts General.....	0.6 %
Marino, ⁵	Brooklyn Hospital	0.6 %

Pathology.—Acute, discrete abscess probably starts as a pyogenic cryptitis at the level of the anorectal line. Edema of the adjacent papilla seals the anal opening of the crypt and so prevents drainage into the rectum. Inflammatory exudate burrows through the sphincter muscles and perianal fat to point eventually as a perianal abscess. It is likely that because of their acute onset, most lesions of this type are primarily pyogenic in origin. Many of them are secondarily infected with tubercle bacilli, thereby becoming contact infections after the abscess ruptures spontaneously or is inadequately drained by incision.

Serpiginous subcutaneous abscesses were more common in our series. The lesion characteristically appears as a widespread chronic subcutaneous induration consisting largely of tuberculous granulation tissue with little pus, the overlying edematous skin colored a livid dusky red. Pathogenesis in these cases consists of a direct spread of contiguous tubercles along the perianal lymphatic network, recently demonstrated by Nesselrod.⁶ This lymphatic network completely circumscribes the anus to empty into collecting vessels running toward the inguinal nodes. Tubercle bacilli from swallowed sputum enter the lymphatics through a break in the epithelium of the anal canal. The infection spreads along the perianal lymphatic network, often extending toward the groin along the course of the collecting lymphatics (Fig. 1). In our series all patients with serpiginous subcutaneous lesions had positive biopsies for tuberculous granulation tissue.

Perianal fistulae occurring in tuberculous patients usually result from previous abscesses. They have at least one external opening on the skin as well as an internal orifice leading into the rectum or anus. Sinuses similarly result from abscesses but differ from fistulae in having but one orifice, either internal leading into the gut, or external opening through the skin. Even in tuberculous individuals these tracts are occasionally pyogenic, providing, however, that the original abscess was nontuberculous. A simple

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pyogenic fistula or sinus may become tuberculous by contamination following prolonged contact with tubercle-laden feces. A tuberculous fistula, characteristically, is seen as an irregularly serrated orifice, widely patulous, surrounded by edematous, inflamed, undermined skin of a livid color (Fig. 2).

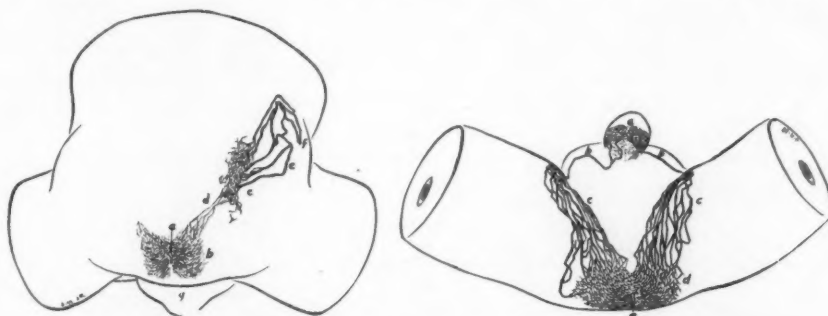


FIG. 1.—Injection of perianal lymphatics of the anal margin. (Left) Perianal and gluteal lymphatics (posterior view) of a male, white fetus at term. Injections made along the anal margin and in the skin over the gluteal region, using mercury. (a) Anus. (b) Network of the perianal skin. (c) Plexus of the skin over the gluteal region. (d) Anastomotic vessels. (e) Collecting vessels. (f) Collecting vessels from the superior gluteal region passing to the groin. (g) Scrotum. (Right) Penile and perianal lymphatics, viewed from below, in the same specimen as that represented in Figure 1 left. Injections made in the skin of the shaft, using mercury. (a) Network of the skin of the shaft of the penis. (b, b) Collecting vessels from the network of the shaft. (c, c) Collecting vessels from the perianal network. (d) Network of the perianal skin. (e) Anus. (Nesselrod, J. P.: *ANNALS OF SURGERY*, 104, 908, Fig. 1, November, 1936.)

Chronic anal fissures in tuberculous patients with positive sputa frequently become contaminated with tubercle bacilli and become tuberculous ulcers. Clinically they appear as anal ulcers, the edges of which are elevated and indurated with dark, violaceous, inflamed epithelial tissue (Fig. 3).



FIG. 2.—External opening of a typical tuberculous fistula.



FIG. 3.—Tuberculous infiltration of a chronic anal fissure.

Lupus or tuberculosis of the perianal skin is seen most frequently in terminal toxic patients in the advanced age group. Our cases were considered inoperable mainly because of extensive destruction of perianal skin and sphincter muscle. Solitary tuberculids are rare and when occurring in the

perianal region are generally regarded as metastatic tubercles. They should be excised.

Diagnosis of Perianal Tuberculosis.—Inasmuch as at least 5 per cent of patients with pulmonary tuberculosis have perianal infections as contrasted against 0.5 per cent of the nontuberculous population (Table III), it follows that perianal infections occur ten times more frequently in tuberculous than in nontuberculous people. In patients with pulmonary tuberculosis, therefore, it is reasonable to expect that most of these perianal infections are tuberculous. Their etiology is dependent on the presence in the feces of tubercle bacilli originally swallowed as tubercle-laden sputum.

In this series, diagnosis of tuberculous perianal infection was based upon the examination of biopsy material obtained at operation showing histopathologic evidence of tuberculous granulation tissue, *i.e.*, typical tubercle formation with central necrosis, fibroblastic capsule, monocytic infiltration and giant cells. Sweany⁷ points out that failure of histopathologic diagnosis in tuberculous perianal lesions depends upon the fact that typical changes are present only in "live granulations." In the taking of specimens, the surgeon should attempt removal of areas of tract containing "live granulations" intact. Often the character of the fistula or abscess affords no granulation tissue. Necrosis, overgrowth of secondary pyogenic invaders with subsequent slough of granulations and fibrosis all tend to change the pathologic characteristics of the original granulation tissue so that even the most experienced pathologist could not venture a diagnosis of tuberculosis. Sweany concludes that "with careful, repeated, or complete samplings, with serial sections and with careful study, over 75 per cent of fistulae and abscesses in tuberculous patients should be found tuberculous. No doubt, all but an insignificant minority are tuberculous."

Recognition of tuberculous perianal lesions by their gross characteristics at operation is, in my opinion, extremely important in attaining even partial cure. The majority of our patients, at the time of operation, had multiple lesions. These consisted of acute or chronic circumscribed abscesses, chronic, diffuse, serpiginous subcutaneous abscesses with fistulae or sinuses. At the margins, or in the depths of the lesion, typical tuberculous granulation tissue was seen. This appeared livid, cyanotic and almost violaceous in color; it was friable, and characterized by absence of free bleeding when wiped away. In patients with subcutaneous serpiginous infection, the tuberculous granulation tissue followed the perianal lymphatic network, frequently extending widely in all directions.

Anesthesia.—Internists have objected to operation in this condition because of the possibility of reactivating the primary disease in the lungs. This was undoubtedly so previously, when ether was employed, with the resultant probability of disseminating tubercle-laden sputum by aspiration into an uninvolved lung region. Local infiltration anesthesia is contraindicated, because of the possibility of disseminating existing infection with the anesthetic solu-

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tion. Caudal and parasacral block is the procedure of choice on our service. Systemic reactions are minimal, and anesthesia complete. The usual technic is employed, namely, 30 cc. of a 2 per cent procaine solution is injected into the epidural canal, and 10 cc. into the second and third sacral foramina on each side. Low spinal anesthesia was employed in a few patients in whom the sacral canal could not be entered. Fifty milligrams of neocaine was the dose required to insure good anesthesia. Premedication consisted of 0.2 Gm. of phenobarbital, two hours before operation.



FIG. 4.—Extensive serpiginous subcutaneous abscess with extension along the inguinal lymphatics. Three weeks after the third stage, showing bilateral inguinal lesions (second stage) almost healed and a bridge of intact skin between the two excised abscess cavities.

Treatment.—The exact procedure used in treating perianal tuberculosis, of necessity, depends on the individual lesion. To cure perianal tuberculous infection, radical excision of the entire pathology is essential. Conservative surgical measures are futile except in individual patients in the terminal stage of pulmonary tuberculosis. The failure of conservative incision is shown by the fact that 35 per cent of the patients in our series had been previously operated upon in other hospitals, with failure of cure even after several years.

As stated, effective operative treatment demands the excision of all perianal tuberculous tissue. Chronic tuberculous lesions tend to extend widely around the anus with multiple fistulous tracts, often with the internal orifice proximal to the internal sphincter muscle. In such cases, good surgical judgment would counsel operation in multiple stages, in order to insure gradual

replacement of excised tissues with blocks of fibrous scar tissue so as to preserve support of the perineal floor. Any uninvolved skin and subcutaneous fat between fistulous or abscessed areas must be saved, as these islands of normal tissue tend to maintain elasticity and minimize distortion due to scar contracture (Fig. 4).

When the internal opening of the fistulous tract enters the rectum through or above the internal sphincter, operation is necessarily performed in multiple stages. The infected perianal lesion is excised widely down to the sphincter but the tract leading through or above the sphincter muscle is left intact. A seton, in the form of heavy silk tape, is passed through the remaining fistula and tied so as to encircle the sphincter muscles. This simplifies identification of the fistula at the time of the secondary revision. The

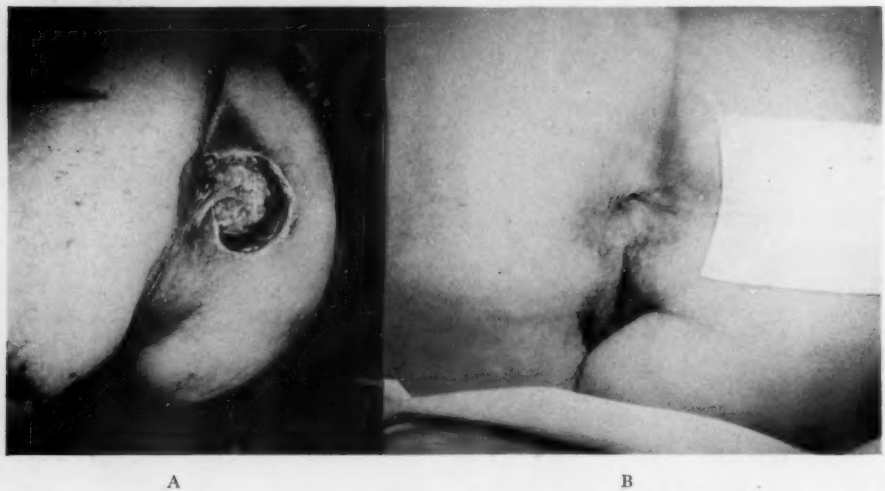


FIG. 5.—(A) Wound after excision of the chronic circumscribed abscess with internal opening of the sinus distal to internal sphincter. (B) Healed scar after eight weeks.

primary wound heals by granulation, so that eventually a wide, gaping perianal wound is replaced by a block of firm fibrous scar tissue adherent, in the anal portion, to the lateral borders of the sphincter muscles. When this has occurred, using the seton as a lead, a grooved director is passed through the remaining fistulous tract and presented externally from the anus at right angles to the direction of the sphincter muscle fibers. The muscle is divided on the grooved director, thereby exposing the remaining fistulous tract which is then excised, leaving a clean "gutter-shaped" wound. Wide retraction of the severed ends of the sphincter muscle is prevented by adhesion of the muscle to the block of scar tissue at the site of the primary operation. By the use of this two-stage method, sphincter function is preserved and incontinence prevented.

When the sphincter muscle itself is widely involved in the lupus type of perianal infection, operation is contraindicated, because extensive excision of sphincter muscle must result in incontinence. Fortunately, these usually

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occur in toxic, advanced terminal cases whose life expectancy is short. My feeling is that a patient is happier with a perianal tuberculous lesion than with an incontinent anus.

Acute abscesses are treated early by adequate incision to drain pyogenic pus. Tuberculous granulation tissue is absent in this early stage. After two to three weeks, to allow subsidence of acute infection, the resulting fistula is excised.

Chronic, discrete circumscribed abscesses in our patients were usually tuberculous. Exploratory incision revealed little or no pyogenic pus, but typical dusky, cyanotic, friable tuberculous granulation tissue was seen comprising the walls of the cavity, with necrotic tissue filling the lumen. The entire lesion was widely excised so that no tuberculous granulations or fibrous abscess wall remained. The resultant wound should be "saucer-shaped," the base consisting of normal healthy subcutaneous fat (Fig. 5). The internal opening of the communicating fistula is simultaneously excised, in the primary stage if it presents below the internal sphincter; or, if proximal to the internal sphincter, by seton and secondary operation as described.

The patients that presented our most difficult therapeutic problems were those with extensive multiple lesions. These consisted of widespread, creeping or serpiginous subcutaneous abscesses, often multiple, the individual abscesses connecting with each other through one or more fistulous tracts. Most of the patients operated upon in other institutions were of this type. They came to us with draining fistulous tracts, which usually communicated with serpiginous abscesses. Multiple operations in successive stages may be necessary when the lesion is extensive. The patient shown in Figure 6 required six stages over a period of 18 months to obtain what is now a two-year cure. Planned procedures in these widespread, multiple lesions must often be altered by findings at operation. The largest area of cyanotic, edematous skin overlying a subcutaneous abscess is incised. The abscess is unroofed by excising the overlying skin, thus affording ample space for exploration. The granulation and fibrous tissue comprising the floor and lateral walls of the abscess are excised. Islands of tuberculous granulation tissue are easily distinguished in the wound by their dusky, cyanotic color. When explored with a probe these granulations usually are found to comprise the lumen of a sinus or fistula connecting with an adjacent abscess, or with an internal or

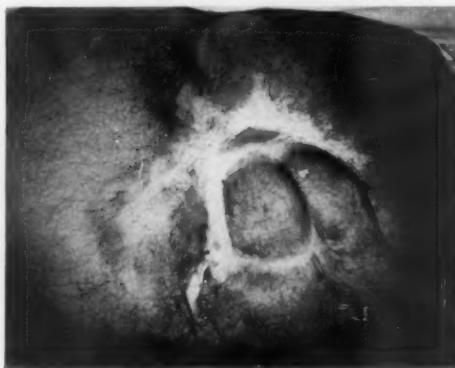


FIG. 6.—Complete healing of extensive perianal abscess with multiple fistulae. Six stages were necessary, over an interval of 18 months. Patient gained 50 pounds and had no recurrence in two years' follow-up.

external fistulous orifice. A grooved director is threaded through the tract, which is exposed by a scalpel incision. As just stated, the tract may communicate with another abscess. The sinus tract and abscess are, therefore, excised, being careful to leave any island of uninvolved skin if possible. If the resulting wound promises to be very extensive, completion of operation is deferred for six to eight weeks to allow healing of the primary wound, in order to insure fibrous support of the perineal floor by formation of a block of scar tissue.

Occasionally, the sinus is seen to lead cephalad into the superior rectal space. In such a case, practicability counsels conservatism, inasmuch as excision of the entire tract would entail sacrificing the supporting muscles of the rectum and would result in a very extensive loss of tissue. Our procedure



FIG. 7.—(A) Extensive abscess widely excised showing the distal aperture of the sinus extending into the superior rectal space. Excision of the tract unfeasible; treated subsequently by chemical cauterization.



FIG. 7.—(B) End-result.

has been to excise the abscess and sinus tract to the level of the floor of the superior rectal space. After two or three weeks, when the wound is granulating well, the remaining sinus is packed with silver nitrate stick. The eschar is removed in 48 hours. Chemical cauterization, as described, must often be repeated, the desideratum being the destruction of the tuberculous granulation tissue. End-results in these cases are satisfactory, inasmuch as the abscess is eliminated and the tuberculous sinus converted into a simple granulating sinus draining serum instead of tuberculous pus (Fig. 7).

Fistulae often extend from the primary abscess, course deep in the subcutaneous tissue to emerge at a distance in a remote external fistulous opening. This tract should be widely excised, excision to include overlying skin and the external orifice. A similar procedure is used when the internal orifice of the fistula emerges in the anus distal to the internal sphincter. The external sphincter muscle is incised over a grooved director passed through the fistula at right angles to the direction of the muscle fibers. If the fistula emerges above or in the internal sphincter muscle, the two-stage excision with seton is used. Multiple combinations of abscesses, external and internal fistulae,

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are commonly seen (Fig. 8). Tuberculous anal ulcers are treated radically. Wide excision of the ulcer and adjacent skin is imperative to prevent extension of the lesion. Healing takes place by granulation and epithelialization.

Cautery excision of tuberculous perianal infection is advocated by some surgeons. Apparent advantages include the sealing of the afferent lymphatics, hemostasis, and complete destruction of tuberculous tissue. Despite these advantages, the cautery knife and curette were soon discontinued as a routine on our service. Their disadvantages, in our experience, consisted in the fact that isolated foci of tuberculous granulations in the wound were obscured by resultant charring. Depth of coagulation of tissue was difficult to control, postoperative slough was extensive and painful, and healing was markedly delayed.

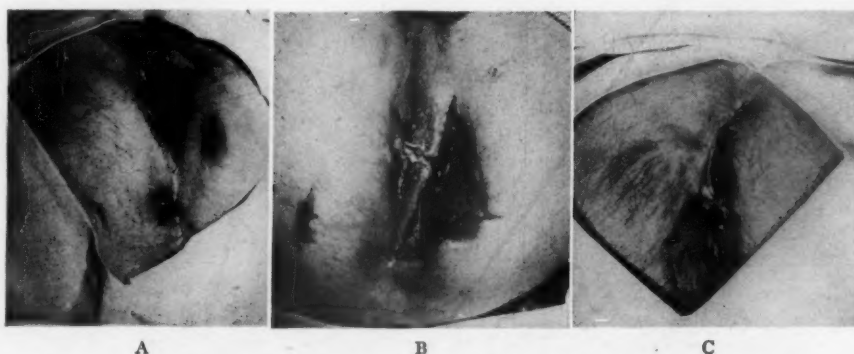


FIG. 8.—Patient operated upon for fistula five years ago. (A) Present status—residual abscess in the left buttock with three external fistulous orifices and one internal orifice above the internal sphincter muscle. (B) Extensive excision of the anterior and posterior fistulous tracts and abscess. Seton shown placed through internal opening above the internal sphincter. (C) After excision of the seton—almost healed.

We do not employ methylene blue to delimit fistulous tracts, as it was found, as shown by Rogers and Hall,⁸ that besides the primary tract, all surrounding tissues became stained. This definitely obscured rather than clarified the dissection of tuberculous tissue.

Elective anal surgery, such as hemorrhoidectomy and excision of simple fissure in tuberculous patients with positive sputum, presents a problem. Of 34 such operations performed on our service, contamination of wound occurred in two patients. Biopsy from the wound margins showed tuberculous granulation tissue. Healing was delayed in four of these cases—one, 20 weeks; two, 12 weeks; and one, eight weeks. Wound contamination with tubercle bacilli in these cases was the probable explanation for delayed healing. The possibility of tuberculous skin infection, unrecognized at the time of operation, is suggested, however, by the histologic finding of tubercles in the routine biopsy of a hemorrhoid from an uncomplicated case who went on to healing in three weeks (Fig. 9).

Postoperative Treatment.—Postoperative reaction was surprisingly moderate considering the fact that large areas of tissue were removed, and

that hemorrhage was fairly profuse in patients with advanced tuberculosis whose general condition was poor. Temperature was slightly elevated for two or three days; pain was moderate and easily controlled by sedation.

At completion of the operation, the wound is packed tightly with iodoform gauze which is removed in 48 hours. Sitz baths are then instituted twice daily, the wound being loosely packed with gauze saturated with cod liver oil. Patients are urged to be ambulatory early, this, however, depending on the extent of pulmonary involvement. Once or twice weekly, granulations are swabbed with pure phenol and when exuberant are first removed with a sharp uterine curette. Following this routine, we have had no contamination of

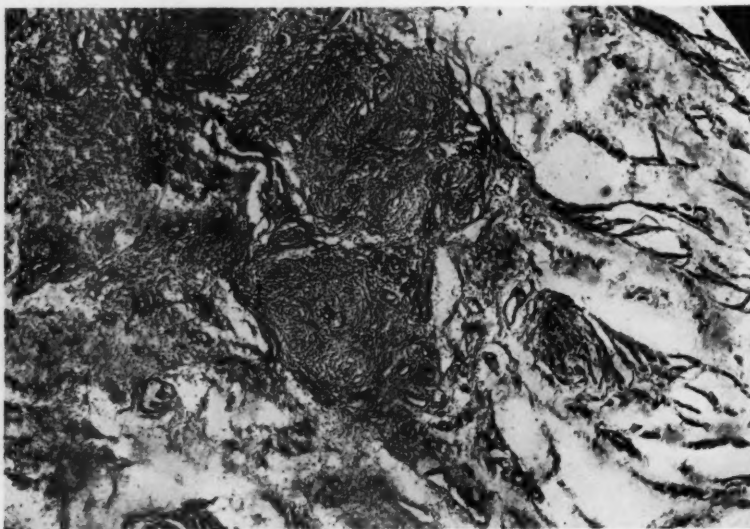


FIG. 9.—Photomicrograph showing two tubercles below the skin in a hemorrhoid of a patient with positive sputum. Preexisting, unrecognized perianal tuberculosis may account for delayed healing of hemorrhoidectomy wounds in patients with active pulmonary tuberculosis.

wounds, and when primary excision has been complete, wounds have healed even in patients with marked pulmonary involvement and with high concentration of bacilli in the sputum. Pinch-grafts were necessary in one patient, in whom epithelialization appeared stationary, because of extensive resection of skin.

SUMMARY.—Table IV gives the results obtained in 100 consecutive patients operated upon between April, 1935, and September, 1939. Considering only the 68 cases with proved perianal tuberculosis (positive biopsy), a number of significant points regarding this clinical entity are apparent (Table V).

In order of frequency, multiple lesions, *i.e.*, abscesses plus fistulae, were most common, 61 per cent; fistulae alone, 21 per cent; acute or chronic abscess, 18 per cent. Operation was necessary in stages in 40 per cent. However, a number of patients upon whom one operation was performed on our service, had been operated upon previously in other institutions, 35 per cent.

PERIANAL TUBERCULOSIS

TABLE IV

RESULTS IN 100 TUBERCULOUS PATIENTS WITH PERIANAL INFECTIONS
TREATED BY RADICAL EXCISION OF LESION

	Positive 68	Biopsy for Tuberculosis Negative 18	No Biopsy 14	No. of Cases
Pathology:				
Abscess.....	12	2	6	20
Fistula.....	14	10	5	29
Abscess plus fistula.....	42	6	3	51
Number of operations:				
1 operation.....	41	13	14	68
2 operations.....	19	4		23
3 operations.....	4			4
4 operations.....	3	1		4
6 operations.....	1			1
Complete healing—in months:				
Less than 4 mos.	33	11	9	53
Less than 8 mos.	14	3	2	19
Less than 12 mos.	1			1
Over 12 mos.	1			1
Unhealed—in months:				
Discharged				
Less than 4 mos.	4	2		6
Less than 8 mos.	2			2
Less than 12 mos.	1			1
Died				
Less than 4 mos.	3	1	2	6
Less than 8 mos.	4		1	5
Less than 16 mos.	1			1
Unhealed: Persistent sinus..	4	1		5
Weight:				
Gain.....	39	6	4	49
Loss.....	10	3	2	15
Stationary.....	19	9	8	36
Sputum:				
Positive.....	62	13	11	86
Negative.....	6	5	3	14

Cure was complete in 49 per cent in less than four months. Healing occurred in 72 per cent of 68 patients with positive biopsy for tuberculosis granulation tissue. Eight patients died and seven were discharged from the hospital with unhealed wounds. Of 53 patients with positive tuberculosis on biopsy, upon whom radical excision was performed, and who remained under our observation in the hospital, 49 (92 per cent) went on to complete healing. Of the remaining four, three patients had persistent sinuses extending into the superior rectal space; the other refused excision of a remaining superficial fistula

which was symptomless. Weight remained stationary in 19 patients in this group, 39 gained weight, and ten lost weight after operation. Positive sputa were present in 91 per cent of this group.

TABLE V

END-RESULTS FOLLOWING RADICAL EXCISION IN 68 PATIENTS WITH
PERIANAL INFECTIONS—HISTOPATHOLOGICALLY TUBERCULOUS

	No. of Cases	Percentage
Pathology:		
Abscess.....	12	18
Fistula.....	14	21
Abscess plus fistula.....	42	61
Number of operations:		
One.....	41	60
Multiple.....	27	40
Complete healing—in months:		
Less than 4 mos.	33	49
Less than 8 mos.	14	21
Less than 12 mos.	1	1.5
Over 12 mos.	1	1.5
	49	72
Unhealed—in months:		
At discharge from hospital:		
Less than 4 mos.	4	6
Less than 8 mos.	2	3
Less than 12 mos.	1	1.5
	7	10
At death:		
Less than 4 mos.	3	5
Less than 8 mos.	4	6
Less than 12 mos.	1	1.5
	8	12
Unhealed: Sinus persists in wound.....	4	6
Weight:		
Gain.....	39	57
Loss.....	10	15
Stationary.....	19	28
Sputum:		
Positive.....	62	91
Negative.....	6	9

CONCLUSIONS

(1) Perianal infections occur in 5 to 10 per cent of patients with pulmonary tuberculosis as contrasted to 0.5 per cent in the nontuberculous population. Tuberculous granulation tissue was found on histopathologic examination in 79 per cent of 86 patients in this series. Fourteen cases early in the series had no biopsy.

(2) Multiple lesions, *i.e.*, abscesses and fistulae, were the most common. Lesions were frequently extensive, and spread usually occurred along the course of the superficial perianal lymphatics.

(3) Conservative surgery is futile in the treatment of perianal tuberculosis, as shown by persistence of pathology in 35 per cent of our patients previously operated upon elsewhere.

(4) Effective treatment demands radical excision of all existing pathology. Foci of tuberculous granulation tissue must be carefully sought for in the wound and completely eradicated when found. Operation in stages is frequently necessary because of the extent of the lesion. Radical procedures as described, when instituted early, should result in a high percentage of cures.

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INTERNAL DERANGEMENTS OF THE KNEE JOINT

AN ANALYSIS OF ONE HUNDRED CASES WITH FOLLOW-UP STUDY

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IN THIS REVIEW of 100 cases of internal derangement of the knee, we wish to point out the relative frequency of the various lesions which fall under this general diagnosis; to detail the symptomatology upon which the diagnosis and operative indications are based; and to give the follow-up results obtained in 95 of the 100 cases. In addition, the operative technic and plan of after-care will be described, as well as the operative complications which have appeared.

Anatomy of the Knee Joint.—The knee, although generally looked upon as a type of hinge joint, differs very materially from the true hinge joints such as the elbow and ankle. The surfaces of the condyles of the femur and the head of the tibia fit very poorly. Only in full extension is there a broad surface contact. In all other positions the articular surfaces meet only at points. The semilunar cartilages deepen the joint cavity of the tibia and accommodate it to variations in contact between the condyles and the tibia. They move backward in flexion to deepen and protect the posterior margin of the tibial head, and in extension "they follow the forward rolling of the condyles and deposit themselves in the anterior joint cavity where they become compressed and give a springy protection to the margins of the joint" (Palmer¹) (Fig. 1). Of the two cartilages, the lateral has the greater range of motion. The movement of the internal cartilage is limited by its wide fixation to the under surface of the internal lateral ligament. It is frequently caught and torn between the internal condyle and the head of the tibia, in movements in which there is internal torsion of the condyles, in the act of extending the knee. In our 64 frank cartilage injuries, 62 were of the internal and only two of the external cartilage.

The synovial membrane is thin. Its chief function is the secretion of synovial fluid which lubricates the joint and nourishes its cartilaginous surfaces. Between the synovial capsule and the infrapatellar ligament is a space filled with a fat pad which, in extension, comes to lie in between the condyles. This pad is believed by many to counterbalance the variations in pressure that occur with changes in the position of the joint. The pad responds to trauma by becoming edematous, and later forms firm fibrous "snow-capped" projections into the joint cavity.

The integrity of this relatively weak articulation is maintained largely by

Submitted for publication May 16, 1939.

DERANGEMENTS OF KNEE JOINT

strong ligaments both inside and outside the joint. The crucial ligaments within the joint prevent abnormal anteroposterior luxation. Outside the joint, the strong lateral ligaments, the fibrous part of the capsule, and the tendinous insertions combine to give extreme strength to a relatively unstable bony articulation. It is probable that internal derangements of the knee joint rarely occur without some injury to the adjacent ligaments. On the other hand, repair of the internal derangement will usually relieve the repeated strains on the ligaments and permit them to regain their normal strength.

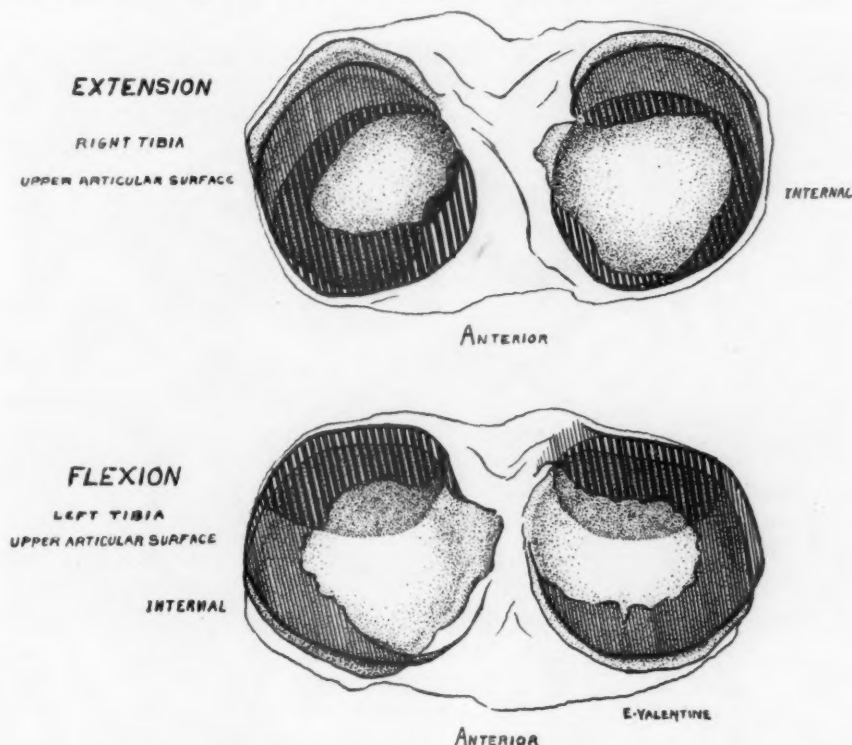


FIG. 1.—Cadaver injection specimen showing position of the semilunar cartilages, and of the articulating surfaces in the right and left knees held in extension and in flexion. The upper surface of the tibia is shown in the drawings, the shaded areas being the area of the articulating surface of the femur on the tibial head. In the upper drawing, in extension, the semilunar cartilages are seen to move forward and the articulating surface is along the anterior portion of the head of the tibia. In the lower drawing, in flexion, the articulating surface of the condyles is seen to be well posterior on the head of the tibia and the cartilages have moved backward away from the anterior edge of the articulating surface of the tibia.

Mechanism of Injury.—The mechanism of injury in internal derangements of the knee joint is similar in almost all cases. The injury is usually indirect in which there is an internal torsion of the femur on the tibia with the knee in partial flexion. In most of our cases, the foot bearing the patient's weight was fixed on the ground and the body and femur twisted either by being struck from the side, as when being tackled or "clipped" in football, or in trying to make a sudden turn while running. This was the mechanism of injury in 65 of our 100 cases. In a smaller group of cases (15 per cent) the same mecha-

nism occurred when the foot and lower leg were twisted with the knee fixed in partial flexion, as in kicking a soccer ball.

It is not surprising that 52 per cent of the injuries occurred in competitive sports, where sudden twists or body blows are not uncommon. Of these, football was the worst offender, accounting for 29 per cent. Basketball, soccer, lacrosse, jumping, baseball, tennis, boxing and wrestling each contributed its quota. Also, naturally, those injuries were more common in males—82 of our 100 cases. Of these, 68 came to operation before their thirtieth year.

FIG. 2.

FIG. 3.



FIG. 2.—Adhesive strapping for the early treatment of internal injury to the knee joint. After aspiration of the effusion, a criss-cross strapping is applied beginning well laterally and as high as possible on the thigh, extending downward across the lower leg at the knee. Several succeeding layers are applied using two-inch adhesive. The straps are anchored above and below by circular turns of elastoplast bandage.

FIG. 3.—Strapping her internal injury to the knee joint. The strapping is completed by the application of a firm elastic bandage at the knee.

Early Treatment.—In none of these cases, except in a few patients who came with the knee locked in partial flexion, was operation advised as a primary treatment. It has been our practice to treat the primary injury by aspiration of the knee and application of a dressing which permits fixation with function. This varied with the apparent severity of the injury. In the milder injuries, fixation was obtained by crossed adhesive strapping anchored above and below by elastic adhesive and held at the knee by an elastic bandage (Figs. 2 and 3). In the more severe cases, a posterior plaster splint was used in some instances and, more recently, a castex case was applied from the ankle to the gluteal fold. It was possible for the patients to be ambulatory with these dressings, which were maintained for three to six weeks. After removal of the

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strap or splint an elastic bandage was used to give partial support to the knee for an additional two to three weeks. If, after a thorough trial at conservative therapy, there were frequent recurrences of knee disability, operative intervention was indicated. The average lapse of time from the original injury to operation was two and one-quarter years.

In our experience, any knee with true locking eventually came to operation. Manipulations under anesthesia, with reduction of the dislocated cartilage or the dislodgment of the foreign body, were followed by recurrence in every case.

In the study of these cases the roentgenogram did not prove of great diagnostic value except in osteochondritis dissecans or foreign body. We were unable to obtain any aid in the differential diagnosis of such difficult lesions as partial cartilage tear and hypertrophic fat pad. Our experience with arthrography has not been great, but we have depended more on clinical findings to interpret the roentgenogram rather than the reverse. Nevertheless, we believe a routine preoperative roentgenogram of the knee is indicated in every case in order that bony injury or foreign body may not be overlooked.

The injuries naturally divide themselves into four main groups according to types of pathology, *viz.*, cartilage injuries; injuries to the synovium and fat pad; crucial ligament injuries; and foreign bodies.

Cartilage Injuries.—Of 100 cases of internal derangement of the knee joint, 65 showed frank injuries of the semilunar cartilages themselves. These were divided into four groups: Longitudinal tears; tears in the anterior portion of the cartilage; tears in the middle portion of the cartilage; and tears in the posterior portion of the cartilage.

LONGITUDINAL TEARS (BUCKET HANDLE)

By far the largest group, 31 per cent of the 100 cases, was comprised of patients having longitudinal tears of the cartilage, mostly of the bucket-handle type. Of these, 21 arose in competitive sports. Thirty of the patients were males. The left knee was involved in 17 cases, the right in 13 cases. The symptoms produced were fairly constant and permitted a more or less accurate diagnosis. There was marked pain in the knee joint, usually on the anterior mesial side, recorded in 27 cases. Effusion was present in almost all cases. Many patients came to the hospital at the time of the original accident with the knee locked. The others gave a definite history of locking at intervals. In a few cases, the dislocation of the torn cartilage between the condyles was reduced by manipulation, but there were recurrences every time. In those cases in which the patient came for treatment at the time of the original injury, the knee was held in partial flexion. It could not be completely extended or flexed, although there was some range of motion in the middle portion of the flexion arc. The most definite complaint was a persistent inability to extend the leg completely, due to the fixation of the torn portion of the cartilage at the anterior horn, preventing complete anterior rotation of the condyles on the

head of the tibia. In one case, a patient who had his knee locked, tripped and fell, tearing loose the anterior portion of the cartilage so that at the time of operation he was able to extend the leg completely, but the cartilage was found lying between the condyles.

The findings on examination in these cases varied a great deal, according to the time at which they were seen. When seen early, an inability to extend the leg completely was noted and usually there was a definite effusion, although this is not invariable. Those patients who were seen late, having had a history of frequent lockings, may have had no effusion whatever, but there usually was a definite area of tenderness at the inner side of the infrapatellar ligament at the head of the tibia. In such cases there may or may not be some relaxation of the lateral ligaments of the joint, especially of the internal lateral ligament. In the 31 cases with longitudinal tears of the cartilage, the correct diagnosis was made in 30 instances. The other diagnosis was incorrect in that the cartilage injured was the external instead of the internal cartilage.

In all cases, the cartilage was removed as far back as possible, removing all of the detached tissue. In one patient who had a history of six years' duration, there was a definite area of erosion of the cartilage over the end of the femur. Twenty-nine of the 31 cases were followed (Table I).

TABLE I

SYNOPSIS OF THE 29 INSTANCES OF LONGITUDINAL TEAR FOLLOWED-UP

15-20 years of age (6 cases; 5 followed)

Result: 4 normal

1 has weakness, stiffness, clicking (this patient had erosion of cartilage along inner condyle at operation)

Follow-Up Period: 3 years 2 cases
4 years 1 case
9 years 2 cases

20-30 years of age (20 cases; 19 followed)

Result: 19 normal (2 have slight ache after extreme exercise)

Follow-Up Period: 1 year 2 cases
2 years 1 case
3 years 2 cases
4 years 4 cases
5 years 10 cases

(No relation seen between duration of symptoms and operative result in this group)

30-40 years of age (5 cases; 5 followed)

Result: 5 normal

Follow-Up Period: 2 years 1 case
4 years 1 case
7 years 2 cases
9 years 1 case

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TEARS OF THE ANTERIOR PORTION OF THE INTERNAL SEMILUNAR CARTILAGE

There were 18 patients in which a tear of the anterior portion of the semilunar cartilage was found. Of these, all but one were males. The history of injury showed competitive sports to be a major factor in the causation. Fourteen tears occurred in this manner, 11 of these in football. The symptoms these patients exhibited were somewhat similar to those sustaining longitudinal tears. At the time of the injury, there was immediate pain and effusion. The knee, however, usually was not locked and, as the effusion decreased, the patient was able to get along for a time without disability. Twists of the knee, however, resulted in a recurrence of the injury characterized by a catching of the torn cartilage between the condyle and the head of the femur. As a rule, true locking did not take place, but the catching of the foreign body gave the sensation to the patient of the knee giving way underneath him, and frequently falls resulted. This symptom was so similar to that described in cases of hypertrophy of the infrapatellar synovium that it was almost impossible to distinguish between these two clinical entities. Occasionally, the torn cartilage would work itself into the space between the condyles, in which case true locking of the joint would take place.

On examination, the chief points of diagnostic importance were the tenderness along the anterior portion of the semilunar cartilage when deep pressure was made, the effusion and the definite crepitation on motion of the joint. We were unable to distinguish with certainty this type of injury from the injuries resulting in contusions of the infrapatellar fat pad, and, in diagnosing these cases, almost invariably, the diagnosis was made of an internal derangement of the knee joint, the type undetermined.

In the treatment of these tears the entire cartilage was removed in 11 cases, and, in seven cases, only the anterior torn portion of the cartilage was excised. Sixteen of the 18 cases were followed (Table II).

TABLE II

SYNOPSIS OF THE 16 INSTANCES OF TEARS OF THE ANTERIOR PORTION OF THE INTERNAL SEMILUNAR CARTILAGE FOLLOWED-UP

Under 20 years of age (5 cases; 5 followed)		
Results: 5 normal		
Follow-Up Period:	7 months	1 case
	4-6 years	4 cases
20-30 years of age (11 cases; 10 followed)		
Result: 10 normal		
Follow-Up Period:	3-10 months	3 cases
	1-2 years	2 cases
	4-6 years	3 cases
	14 years	2 cases
30-40 years of age (1 case)		
Result: normal		
Follow-Up Period: 1 year		
40-50 years of age (1 case; not followed)		

In this group of cases, we were interested to note whether there was any improvement in the follow-up results in those knees in which only the anterior torn portion of the cartilage was excised over those who had the entire cartilage removed. As a matter of fact, in the entire follow-up group, all the knees were normal, indicating that a conservative operation, with simple removal of the torn portion of the cartilage, will give an excellent result (Fig. 4).

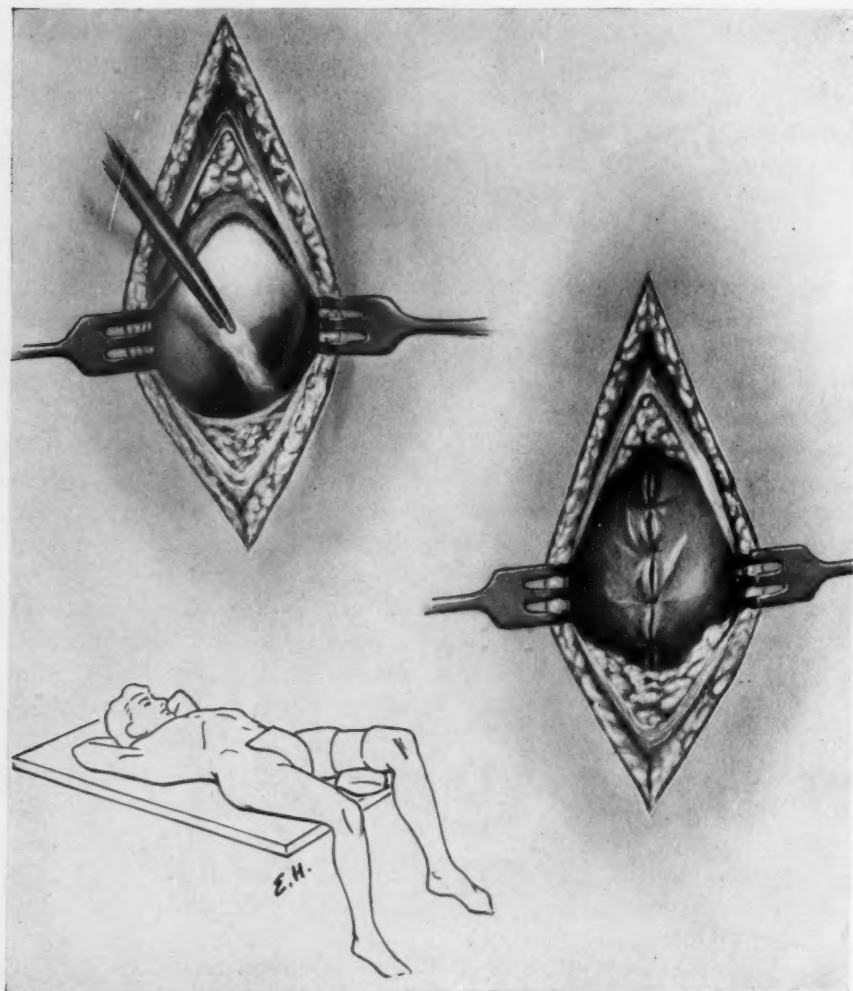


FIG. 4.—Upper drawing: Case showing a dog-eared tear of the anterior portion of the cartilage. In seven patients, only this torn portion of the cartilage was removed. Good results were obtained in all instances.

Middle drawing: Showing method of loosely suturing the capsule of the joint with interrupted sutures. The loose suture permits escape of joint effusion and so prevents secondary effusions of the knee after operation.

Lower drawing: Showing position of the patient on the table, sand-bag under the knee and tourniquet on the thigh. It is to be noted in these drawings that the wound covers, which are clipped to the skin edges with Michel clips, have been omitted.

TEARS OF THE MIDDLE PORTION OF THE INTERNAL SEMILUNAR CARTILAGE

There were ten cases in which only the middle portion of the semilunar

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cartilage was injured, either by a transverse fracture of the cartilage or by a dog-eared tear. All of these patients were male. Three of the injuries occurred in football.

There were pain, effusion and intermittent catching or locking in the knee joint in practically all cases. The patient, almost invariably, complained of a sensation of the knee giving way, and recurrences of the disability were quite frequent. We were unable, from physical examination, to make a definite diagnosis in this group. The symptoms were almost indistinguishable from those described for anterior tears of the cartilage, although it is possible that the area of tenderness on pressure over the cartilage was more lateral than noted in the anterior group. In all cases, the cartilage was excised as far back as possible. All ten cases were followed (Table III).

TABLE III

SYNOPSIS OF THE TEN INSTANCES OF TEARS OF THE MIDDLE PORTION OF THE INTERNAL SEMILUNAR CARTILAGE FOLLOWED-UP

Age	Patients	Result	Follow-Up Period
20-30 years	6	5 normal 1 has occasional effusion and locking	2, 4, 10, 13, 14 years 6 years
30-40 years	2	Normal	1, 6 years
40-50 years	1	Has slight limitation of flexion	8 years
Unknown	1	Normal	5 years

POSTERIOR TEARS OF THE SEMILUNAR CARTILAGE

There were six cases in which a tear of the posterior portion of the semilunar cartilage was noted at operation. Of these, five were males. The one female patient sustained her injury playing hockey. Three other cases received theirs in athletics. Again, we were unable to note any characteristic symptomatology in patients with posterior tears of the cartilage. The symptoms of pain along the inner side of the knee with effusion, locking or catching and giving way were constant in this group. The findings on examination were also similar to those described for anterior tears. There was usually pain on twisting of the leg with tenderness along the inner side of the patellar ligament. In our analysis, there were no characteristic symptoms which would permit a diagnosis of the position of a partial tear of the cartilage. Furthermore, the diagnosis was by no means easy at the time of operation. It is the suspicion of the presence of these partial tears which accounts very often for removal of the cartilage when no injury to the cartilage can be found at the anterior portion of the joint. In one of these cases, the cartilage appeared to be normal and was left in place. It was necessary to reoperate upon this patient and remove the cartilage because of recurrence of symptoms. At the second operation, a longitudinal posterior tear of the cartilage was demonstrated. All six cases of posterior tears were followed (Table IV).

TABLE IV

SYNOPSIS OF THE SIX INSTANCES OF POSTERIOR TEARS
OF THE SEMILUNAR CARTILAGE FOLLOWED-UP

18 years of age (1 case)

Result: Feels knee is going to fall apart (has tear of
lateral ligament also, but refuses operation)

Follow-Up Period: 7 years

20-30 years of age (4 cases; 4 followed)

Result: 4 normal

Follow-Up Period: 6 months, 1, 2, 11 years

37 years of age (1 case)

Result: Normal

Follow-Up Period: 2 years

LOOSE INTERNAL SEMILUNAR CARTILAGES

There was a further group of 13 cases in which, at operation, no fracture or dislocation of the semilunar cartilage was found, but there was a very definite looseness of the cartilage (looser than the operator considered normal), and in some of these cases a definite tear of the coronary ligament was demonstrated. These patients frequently had, in addition, definite hypertrophy of the infrapatellar fat pad and adjacent synovium. The question as to whether the looseness of the cartilage produced the disability in the knee joint or whether the hypertrophied fat pad was the cause of the symptoms is still undecided. In this group, there were seven males and six females. Six of the injuries occurred in football, one in boxing, one in tennis and one in tap dancing. The history of these patients was similar to that given for the partial tears of the cartilage. In 11 patients, there was a definite history of pain with effusion in the knee joint. The effusion gradually subsided, but there remained a limitation of extension in some cases, a crepitation in a few. In eight patients there was a history of the leg giving way, and in eight there was a definite history of recurrence of symptoms following a twist of the knee. On examination, the patients presented pain on the inner side of the patellar tendon with tenderness on pressure over that area. There was usually some slight fulness of the knee if the patient was seen soon after an injury or a recurrence. There were no other characteristic diagnostic symptoms. As a result, the diagnosis of internal derangement of the knee joint was usually made because a definite pathologic diagnosis was almost impossible from an examination of the patient or a history of the course of his disease.

Eight patients were treated by excision of the cartilage and the hypertrophied fat pad. In four cases, the cartilage alone was excised and, in one case, an attempt was made to suture the coronary ligament at the site of its injury. All of these patients have been followed (Table V).

In reviewing the follow-up results in this group of cases, we have reached the conclusion that in those patients in whom the internal semilunar cartilage appears loose, but in whom there is also a definite hypertrophy of the synovial

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TABLE V

SYNOPSIS OF THE 13 INSTANCES OF LOOSE INTERNAL SEMILUNAR CARTILAGES FOLLOWED-UP

Under 20 years of age (2 cases)

Result: 1 has slight swelling (coronary ligament sutured at operation)

1 has weakness, swelling, giving way, crepitation (fat pad not removed)

Follow-Up Period: 1 and 2 years

20-30 years of age (8 cases)

Result: 8 normal

Follow-Up Period: 3-6 months 2 cases

1 and 2 years 1 each

5-7 years 4 cases

Over 30 years of age (3 cases)

Result: 2 normal

1 not quite normal (fat pad not removed)

Follow-Up Period: 1 year 1 case

2 years 2 cases

infrapatellar pad, an excision of the fat pad should be performed as well as removal of the cartilage. As a matter of fact, it is our belief that in all probability the causation of the symptoms in these patients is more often due to the hypertrophied fat pad than it is to the looseness of the internal semilunar cartilage.

HYPERTROPHY OF THE INFRAPATELLAR FAT PAD (SYNOVITIS)

The second group of cases of internal derangements of the knee joints showed a definite hypertrophy of the infrapatellar fat pad without any injury

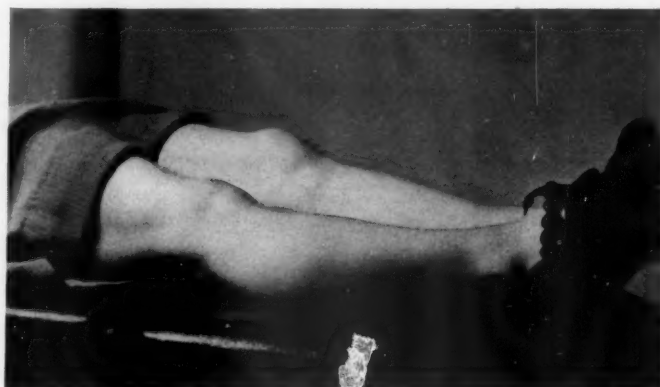


FIG. 5.—Patient showing the limitation of extension in hypertrophy of the infrapatellar fat pad.

to the cartilages of the joint. In this group were 16 cases, nine of whom were males and seven females. Nine gave a history of having had a twist when falling. Four of the injuries occurred in sports. Pain and effusion were present in all cases. In addition, there was a history of limitation of extension

in most cases (Fig. 5). The sensation of giving way was a frequent symptom, and recurrences were quite the rule. Many of these patients gave the history of pain, especially on going up and downstairs, more frequently on going downstairs when they put the affected leg down and began to bear their weight on that leg. Most of them complained of pain on slight twists of the knee. On examination in the acute stage, there was definite effusion with tenderness on either side of the patellar ligament. There was perhaps a more marked fulness on each side of the ligament in these patients, although this finding was a relative one and somewhat difficult to demonstrate clinically. In the quiescent stage, the area of tenderness was closer to the patellar tendon than was present in the cases of anterior tears of the semilunar cartilage, although this finding also was difficult to be sure of in a clinical examination. In those cases in which there was a definite hypertrophy of the infrapatellar pad, there was oftentimes a slight limitation in extension as compared to the normal, but in some cases this finding was quite indefinite. These patients were operated upon with the diagnosis of chronic synovitis in six of the 16 cases; in five cases, an indefinite diagnosis of internal derangement of the knee joint was made and, in four cases, a definite diagnosis of fracture or dislocation of the internal semilunar cartilage was made. It is obvious that the diagnosis of this lesion was a great deal more difficult than the diagnosis of a fracture of the semilunar cartilage. There did not seem to be any definite clinical finding present on examination which would make a certain diagnosis possible.

At operation in 12 of these cases, the fat pad was excised. In two, a complete and thorough examination of the joint was made and the joint closed without any intra-articular surgery. In one case, the internal semilunar cartilage was removed in the fear that there might be a posterior tear of the cartilage. In another, which was an operation for recurrence, a foreign body was removed in addition to some of the hypertrophied synovium. Of these 16 cases, all but one were followed (Table VI).

TABLE VI

SYNOPSIS OF THE 15 INSTANCES OF HYPERTROPHY OF THE INFRAPATELLAR FAT PAD (SYNOVITIS) FOLLOWED-UP

Under 20 years of age (4 cases; 4 followed)

Result: 3 normal

1 has slight weakness

Follow-Up Period: 6 months-1 year

2 cases

3 years

1 case

5 years

1 case

20-30 years of age (8 cases; 7 followed)

Result: 4 normal

3 fair

Follow-Up Period: 2-8 months

3 cases

2 years

2 cases

3 years

1 case

7 years

1 case

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TABLE VI—(Continued)

30-40 years of age (3 cases; 3 followed)		
Result: 3 normal		
Follow-Up Period: 6 months		1 case
2 years		1 case
9 years		1 case
51 years of age (1 case)		
Result: slight pain on extension		
Follow-Up Period: 6 months		

In the three cases in the 20-30 age group considered to have fair results, there is a recurrence of swelling upon twisting the knee and an occasional sensation of giving way. One patient, who had had two previous operations in which both cartilages had been removed, had developed a hypertrophic synovitis with the appearance of a foreign body. The foreign body was removed and the hypertrophic synovium excised, and this patient still has a slight ache in the joint operated upon, with some crepitation. However, he works as a lifeguard and has a fairly normal knee. In this case, we had an opportunity to observe the area of the semilunar cartilages some years after their removal. There was an apparent regeneration of the cartilage, or of fibrous tissue in place of the cartilage, which served to take its place fairly well.

These cases with hypertrophy of the infrapatellar fat pad and those with loose internal semilunar cartilages are hard to diagnose and it is difficult to determine what treatment should be given. In the former group, we excised the cartilage in 12 of the patients, and in those cases a relatively good follow-up result was obtained. However, in two cases, we closed the knee without any operative intervention whatever, and both of these cases have shown excellent follow-up results. This leads us to speculate as to whether the operation of removal of the hypertrophic fat pad is the essential factor in producing a good knee, or the operation, by producing scar tissue and tightening up upon the fibrous capsule of the joint, has produced the good result. Too, the period of three to four weeks of relative immobilization may be sufficient to produce a subsidence of the edema and swelling of the fat pad which would remove the obstructing tissue and thereby relieve the disability.

INJURIES TO THE CRUCIAL LIGAMENTS

There were four patients who had injuries to the crucial ligaments. All of these were males. Three of the injuries occurred in football, and one patient gave the history of an injury the result of wrenching the leg. Pain and effusion in the knee joint were present in all cases. There was some limitation of motion in two. There was a sensation of giving way in the knee in two cases, and in all there were recurrent attacks of disability in the joints following twists. In none of these cases was there any particular laxity on anterior or posterior motion of the leg on the femur, and in no case was there a diagnosis of a tear of the crucial ligament made before operation. As a matter of fact, all were operated upon with the diagnosis of internal derangement of the knee joint. At operation, injury of only the anterior crucial ligament was found. In one case the ligament was partially torn and in the others it was

completely torn across. In two patients there was also a tear of the internal semilunar cartilage and in one there was a definite hypertrophy of the infrapatellar fat pad. It is questionable whether the tear of the ligament was accountable for the patient's symptoms in any of these cases.

At operation, the torn cartilage was excised and the torn ligament trimmed in two cases. In the third case, the hypertrophied fat pad was excised and the ligament was trimmed, and in the fourth there was an attempt made to repair the torn ligament. Three of these patients were followed, one for five and two for two years. All of these patients presented normal knees. They stated they are able to enter into sports without difficulty although two occasionally wear elastic knee-caps when engaging in strenuous sports.

OSTEOCHONDRITIS DISSECANS AND FOREIGN BODIES IN THE KNEE JOINT

There were five cases in which the diagnosis of osteochondritis dissecans was made or in which there were foreign bodies in the knee. All were males and, except in one case, there was definite history of injury. In one instance there was a history of direct trauma. In three others the injury occurred in football or basketball.

The symptoms were similar to those that have been characteristic of the other lesions of the knee joint—pain, effusion and crepitation. Locking was present in two cases, and there were numerous recurrences of disability in all. In these cases, more than any other, the roentgenogram is helpful in making the diagnosis. In two of them the roentgenogram was negative, in two, a definite area of rarefaction along the inner condyle was found, and in one case definite foreign bodies were demonstrated in the knee joint. The diagnosis was made on the basis of the roentgenogram in three cases. In the other two cases, in which the roentgenograms were negative, the diagnosis was internal derangement of the knee joint.

The physical signs differed in no respects from those present following injury to the cartilages or hypertrophied fat pads. When locking occurred, as it did in one patient, it was more frequently complete, with absolute immobility of the knee joint, than is the case in tears of the internal semilunar cartilage of the bucket-handle type. Otherwise, the symptoms of pain and tenderness on pressure along the internal aspect of the infrapatellar ligament were the outstanding clinical findings.

At operation, in one case, multiple small fragments of cartilage were removed as well as the internal semilunar cartilage. In two cases, definite joint mice were removed and the hypertrophied infrapatellar fat pad was also excised. In one of these, a definite loose area of cartilage was removed from the mesial side of the internal condyle. In another case, although there had been a diagnosis of osteochondritis dissecans made roentgenologically, no area of loose cartilage and bone was found in the condyle.

The operator simply clipped some synechia extending between the joint capsule and the edge of the condyle of the femur. In one case, there was a recurrence of the foreign body. This was definitely a case of joint mice due to synovial osteochondromatosis. The results in these five cases are relatively

good. In four cases the joint is normal three, four, five and 12 years after operation. In one case there is a fair result, although the patient says he still has a catch but no swelling in his joint. He shows a very good knee on examination. He is a contestant in a compensation claim which may be a factor in his disability.

COMMENT.—Of the 100 patients operated upon for internal derangement of the knee joint, 96 have been followed-up and, of this number, only one is not satisfied with the result. This patient says he feels as if his knee were going to fall apart, which adequately describes his condition, as he has a definite relaxation of his lateral ligament which should be repaired. With the poor result following his previous operation, however, he is unwilling to undergo further operative intervention.

Frequently, it is asked whether operation upon the knee joint does not result in a stiff knee or in the development of a chronic arthritis. It is impossible to answer this question absolutely, but the follow-up results in this series of cases would permit one to feel that the answer should be in the negative. Many of the patients in whom a poor result was predicted have obtained an excellent functional and anatomic knee. In some cases, there has been a period of six months to a year in which some amount of disability in the knee has persisted, but this disability has gradually disappeared and a normal knee function obtained. The age of the patient at the time of operation or the duration of the symptoms did not seem to materially influence the end-result unless there were associated changes in the articular cartilages of the femur.

As to the question of arthritic changes in the knee joint, there is only one case in which any evidence of this type of change has appeared. This patient had been operated upon twice previous to his coming to the University Hospital, and the internal and external semilunar cartilages had been removed. Because of persistence of his symptoms, he was operated upon again, at which time, there was a definite panus above the condyles of the femur and evidence of an hypertrophic arthritis along the edges of the condyle. He later developed a foreign body in the knee joint. This was removed, and since that time his knee function has been good, although he still has slight discomfort. It should be pointed out that in these operations on the knee, definite changes in the cartilage over the condyle of the femur had been seen in three cases, and there was an osteochondritis dissecans apparent at the time of operation in three others. It would appear, therefore, that the operation does not necessarily produce arthritic changes but that the injury to the joint and cartilage and the persistence of disability in the knee joint may be factors in the production of an arthritis if the arthritis does appear (Fig. 6).

The Operative Procedure.—In preparation for operation no special pre-operative technic is used other than that ordinarily employed for any celiotomy. Spinal anesthesia was employed in the large majority of these cases and was found extremely satisfactory for this type of operation. As a rule, no more than 100 mg. of procaine is necessary, and frequently a unilateral

anesthesia may be obtained. A rubber band tourniquet is applied, beginning at the toes and extending upward to the thigh where it is fixed as a circular tourniquet with several layers. The band is then removed from the foot and leg and a cadaveric anemia is produced. The skin is prepared by one application of an antiseptic solution. The patient's knee is bent over a break in the table. The lower leg is wrapped in a sterile sheet bandaged in place so that it can be manipulated throughout the operation at the will of the operator. An incision about two inches long is made, beginning at about the middle of the patella to the mesial side and extending downward

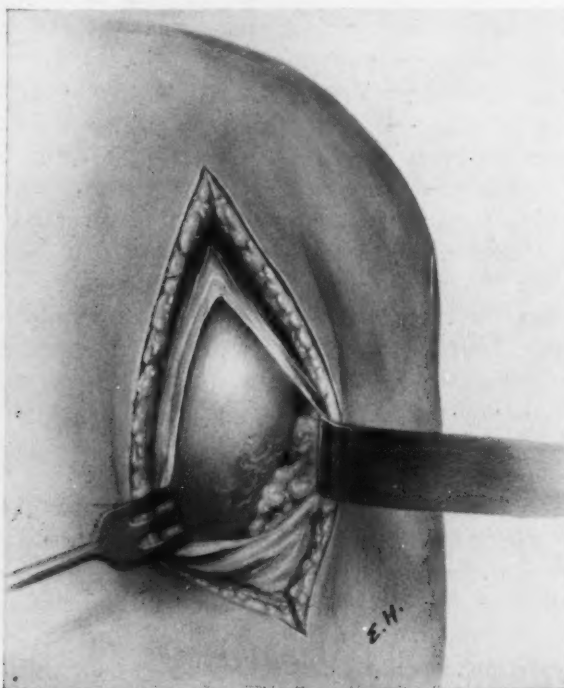


FIG. 6.—Drawing showing marked hypertrophy of the infrapatellar fat pad with erosion of the adjacent cartilage on the condyle of the femur. Duration of symptoms in this case—one year. Erosion of the cartilage on the head of the tibia was also noted in this case.

over the head of the tibia. After incision of the skin and superficial fascia, towels are applied with Michel clips, and the wound is thus protected from skin contamination. After changing knives, the incision is continued through the capsule, thus opening the joint. As a rule, the Lane technic is employed. An aspirator is used for removal of the joint fluid and whatever blood may appear, although bleeding is almost absent throughout the entire operation. Through this opening, the exposure is sufficient to permit inspection of the mesial side of the joint and, if necessary, the incision may be continued upward to dislocate the patella. We have found the curved No. 12 Bard-Parker knife to be extremely useful in excision of the semilunar cartilage. With this knife the excision may be carried around the condyle of the femur

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and then by constant tension upon the loose cartilage, it may be brought underneath the condyle and so almost completely removed. In our experience, it has been found unimportant to remove the extreme posterior corner of the internal semilunar cartilage since this area never gives subsequent trouble in the joint. The hypertrophic fat pad is removed by grasping it with a hemostat or forceps and excising it with the curved knife. Rarely is there sufficient bleeding after this procedure to necessitate ligature, although occasionally a fine catgut suture has been employed to unite the severed synovial membranes.

In closure of the joint, we have followed Böhler's² suggestion not to make a complete and snug suture of the synovial capsule. This is done purposely with the idea that postoperative effusion in the joint can thus be prevented. The infrequency of effusion following these operations has proven the value of this procedure. The fascia in front of the joint is then firmly united with interrupted catgut sutures. At times, it is possible to overlap this structure and so produce a tightening of the fibrous capsule along the inner side of the joint. It is possible that this procedure may account for some of the beneficial results obtained in these operations. Wound closure is accomplished with clips.

For a time, all of these operations were followed by the application of a posterior plaster splint. Recently, the splint has been dispensed with and a simple pressure bandage applied, usually one layer of cotton batting extending for about six inches above and below the knee overlaid with a firm gauze bandage fixed in place with adhesive. The results, as far as effusion or end-result are concerned, have been equally as good with this method of treatment as with the more cumbersome splint application. The patients are kept in bed for two to five days. The average in the 100 cases has been 4.7 days. As a rule, the skin clips are removed on the fifth day and the patient allowed out of bed with crutches. The pressure dressing is continued by the application of an elastic bandage and the patient is encouraged to assume gradually normal weight-bearing on the leg. The crutches are usually continued for about two weeks after discharge from the hospital, after which time they may be dispensed with. The elastic bandage, however, is continued for at least three weeks after leaving the hospital. Many of these patients are back at their normal activities, with normal knee function, within three to four weeks following operation.

In the 100 cases operated upon there were ten wound complications. Seven of these were small serum collections or hematmata, and three were small stitch abscesses. Effusion in the knee joint necessitating aspiration occurred in two cases. There were other minor effusions which were not treated. There were two cases with respiratory complications, and no deaths.

SUMMARY AND CONCLUSION

(1) Internal derangement of the knee joint is usually caused by an internal torsion of the femur on the tibia with the knee in partial flexion.

(2) Eighty-two per cent of our patients were males, and in more than

half of our cases the injury occurred as an accident of competitive sports.

(3) Longitudinal tears of the internal cartilage were the most frequent injury (31 per cent). Removal of the cartilage resulted in a normal knee in 28 of 29 cases followed-up.

(4) Tears of the anterior portion of the cartilage were found in 18 patients. There were 16 patients followed; all have normal knee function. The results are equally good with partial or complete excision of the cartilage.

(5) Tears of the midportion of the cartilage occurred in ten patients. Eight patients followed have normal knee function after excision of the cartilage. One has slight limitation of flexion, and one has occasional catching and effusion.

(6) Posterior tears of the cartilage occurred in six patients. Five patients have good function of the knee after removal of the torn cartilage. One patient has a poor result because of definite relaxation of the ligaments of the knee.

(7) Abnormal looseness of the internal semilunar cartilage was found in 13 patients. In most of these cases there was also a hypertrophy of the infrapatellar fat pad. Excision of the internal cartilage, with or without excision of the hypertrophied fat pad, was performed. In ten patients the knee function is normal. In three cases, in which the fat pad was not excised, there is slight residual disability.

(8) Hypertrophy of the infrapatellar fat pad was found in 16 cases. In 15 cases followed, ten patients have normally functioning knees and five have occasional disability on twisting the knee. In two of the good results the fat pad was not excised.

(9) Injuries to the anterior crucial ligament occurred in four cases. In only one of these was an attempt made to repair the ligament. Good results were obtained in all cases.

(10) Osteochondritis dissecans or foreign bodies were found in five cases. Four of these have good results; one patient has slight residual disability.

(11) A plan for operation and after-care is described in which the essential points are: No special preparation of the knee; spinal anesthesia; bloodless field; loose suture of the synovial capsule; pressure bandage without splint; early ambulatory after-care with early weight-bearing.

Conservatism, aspiration and fixation with function should be employed as a primary treatment. Recurrences of knee disability, especially locking, effusion and giving way, are indications for arthrotomy.

The authors wish to acknowledge with thanks, the privilege of reporting some cases from the services of Doctors Eliason, Muller and Ravdin at the University of Pennsylvania Hospital, Philadelphia, Pa.

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SOME PHYSICAL FACTORS REGARDING CATGUT LIGATURES AND CATGUT KNOTS

A PRELIMINARY REPORT

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THE CONCENTRATION of thought since the work of Lord Lister on the sterilization of catgut appears to have been directed toward the sterility, physical chemistry and tensile strength of the material. Some simple and elementary factors regarding the proper application and the nature of absorption or hydrolysis, *in vivo*, seem to have been almost entirely overlooked. In 1922, the author reported a method of intestinal anastomosis, the principal feature of which is the occlusion of the diaphragms of severed intestine during the completion of the anastomosis by using purse-string sutures with releasable knots. Elementary information, derived concerning the reliability of the release knots in that operation, stimulated further studies on catgut knots and sutures. A very complete review of the literature upon the subject has been presented by Bulloch, Lampitt and Bushill² (1929) and Rhodes, Hottenstein and Hudson¹⁶ (1937). Taylor¹⁷ (1938) is the first to report on thorough experimental work on catgut knots.

Absorption or Hydrolysis of Catgut.—The varied and divergent results of different experimenters make it important to review some of the reports. Callender³ (1874) found a diminution in the size of catgut 24 hours after implantation in the tissues. Reduction to threads was noted in 45 hours, while loops had given way in 60 hours. Macewen¹⁴ (1881) observed that chromic catgut became softened in 14 days, on an average, with a minimum of nine days and a maximum of 19. Claudius⁴ (1906) implanted some of this material in various tissues of rabbits. In the eye, absorption took place without evidence of cellular activity or leukocytic emigration. He believed that the same thing occurred in the peritoneal cavity. Iodine sterilized catgut was absorbed more quickly than carbolyzed but more slowly than that which had been sterilized by dry heat. He stated that iodine catgut disappeared in the anterior chamber of the eye within six days. He also concluded that leukocytic reaction, when it occurs, is mainly due to the chemical difference between the catgut and the surrounding tissue. Ilyin¹¹ (1908) stated that catgut lost its continuity in five days when buried in the superficial layers of the skin. In deeper layers of tissue iodine catgut ligatures were dissolved in seven days and heat sterilized material in six days. In the linea alba the continuity was lost in 14 days and no traces were found after 30 days. In muscle tissue, heat sterilized material was destroyed in seven days while iodine treated catgut lost its continuity, only, in 14 days. In entero-enterostomy both heat and iodine treated catgut lost

Submitted for publication March 24, 1939.

its continuity in six days. Number 3 catgut of both types inserted into the submucosa was absorbed in two to three days. The actual changes preceding the disappearance were slight swelling and loose texture. Goris and Roland⁵ (1917) concluded that the treatment of catgut with chemicals does not necessarily increase the durability of the material. Macrophagic penetration takes place along the fissures of torsion. The rapidity of absorption depends primarily on the physical rather than the chemical treatment of the material. In the less adherent material absorption occurs more rapidly.

Bulloch *et al.*² state: "The manner of experimentation, the preparation of the catgut, the tissues into which the catgut has been implanted and the animal have been varied. . . . The study of the literature on catgut gives no support for the statements that catgut persists for 20, 30 or 40 days in the body, as so many manufacturers of catgut assert."

Very little information is to be found on the absorption of catgut in terms of its tensile strength, except in the writings of Booth¹ (1894), Phillips¹⁵ (1914), Howes¹⁰ (1928), Kraissl and Meleney¹³ (1934), Rhodes, Hottenstein and Hudson¹⁶ (1937) and Jenkins¹² (1937).

Some Physical Factors on the Preparation, Application and Absorption.—The divergent reports and controversies about catgut as a suture material are, no doubt, in many instances due either to the particular method of preparation or, perhaps more so, to the faulty application of the material.

Bulloch and his coworkers² (1929) have made many extensive studies on various physical constants, such as the number of twists per inch of the catgut ligature and their relation to the tensile strength of the material. Other physical factors in their work are quoted in certain experiments with iodized catgut where it has been wound on glass tubes. "This was done because of the possibility of the aqueous solution causing the ligature to untwist." Their results show very conclusively that ligatures wound on glass tubes are distinctly stronger than those which have not been wound. The ligatures which were simply looped were found to swell and even after remaining in the alcohol-glycerol solution for some time they were still about one size larger than the original grade. An examination of the ligatures which had been wound on the tubes showed that they had not swollen appreciably but they had become rather square in cross section, suggesting that they had shrunk and become compressed on the tube. These results confirm previous conclusions that it is important that the ligatures should be under tension during sterilization. It was evident in this last experiment that the ligatures not under tension had swollen considerably and consequently the length decreased.

Among other things, the reliability of the material depends upon the rate of absorption and largely upon the reliability of the knot. The tying of a knot is, after all, a matter of increasing the twist. It is a very exacting procedure of simple detail. Maximum efficiency can be gained only by the use of the so-called reef or square knot. There is but one general method to tie this knot so that the twist in the catgut suture material shall be re-

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tained, if one takes into consideration that the material, as a general procedure, is spun in the clockwise direction. The method is demonstrated in Figure 2.

We believe the most important factor in the absorption of the material is the loss of retention of the twist in the catgut. Certain experimental and clinical data are presented herewith to demonstrate the influence of the twist upon the absorption of the material and the reliability of the knot in the catgut ligatures.

FIG. 1.

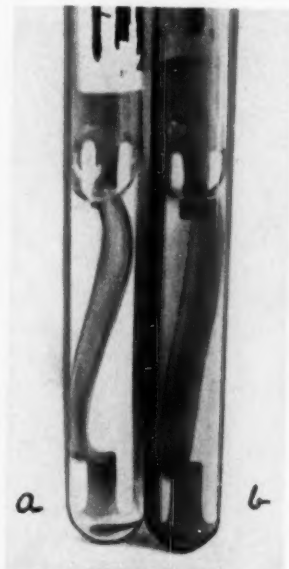


FIG. 2.

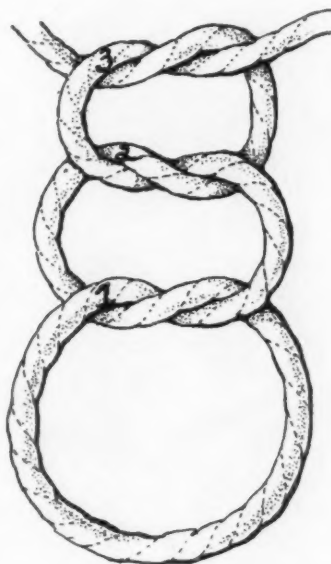


FIG. 1.—Photograph of a tube of No. 1 plain (a) and a tube of No. 1 chromic (b) nonboilable catgut of a popular brand. Note the counter-clockwise twist in this conventional method of winding. The resultant loss of twist exposes more surfaces of the material to the effect of the tissue juices, consequently a more rapid hydrolysis.

FIG. 2.—Triple-throw square or reef knot. The first throw (1) is in the "right hand" or clockwise direction, corresponding to the direction of the twist in the conventionally twisted catgut. This throw should be tied with sufficient tension so as to barely approximate the tissue margins. The second throw (2) is applied in the "left hand" or counter-clockwise direction. It is tied with pressure sufficient to lock the first throw. The third and final throw (3) is tied in the clockwise direction as in the first loop. It may be tied with considerable tension.

This is the ideal catgut knot. It should be used consistently in clockwise spun material. The first or original throw of a catgut knot should never be applied counter-clockwise to the twist in the ligature material.

Experimental Observations.—The exposure of catgut to boiling temperatures, in the presence of moisture, converts the collagen into gelatin, with a consequent loss of tensile strength. The surgeon receives the nonboilable material after it has been dehydrated, sterilized and packed in a storage solution containing a small amount of moisture. It absorbs additional moisture from the tissues when introduced into the wound. This absorption causes a swelling of the catgut in its transverse diameter and produces, to a varying degree, a loss of twist in the material. The loss of twist or separation of strands exposes more surfaces of the ligature material to the in-

fluence of tissue juices. A more rapid dissolution of the material may then be expected.

Of the many methods of winding and packing the material, the most effective is the winding of the catgut on a cone-shaped instrument or tapered bobbin. In our experiments, the material was wound transversely to the instrument in smoothly curved, compact spirals beginning at the base of the bobbin and continuing from this point to the apex of the cone. Care has been taken also to twist the catgut clockwise upon its long axis as it is

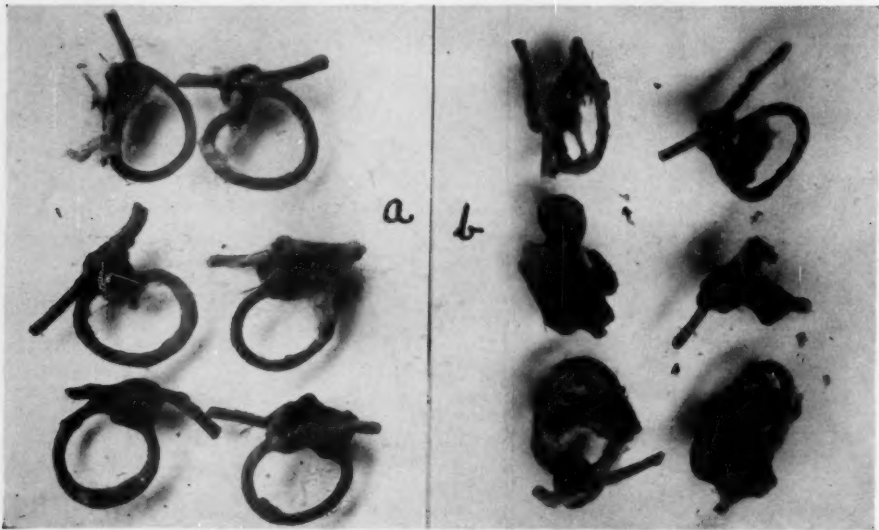


FIG. 3.—Photographs of knotted loops of catgut after they had been imbedded in the abdominal wall of a guinea-pig for 96 hours. All of the knots were tied under five pounds' tension before introduction into the wounds. All of the loops were taken from the same 60-inch strand of material: (a) From the conventionally wound material, and (b) from the spirally wound catgut on a cone-shaped bobbin.

Note the increased diameter of the material: (a) Swelling is probably due to more rapid absorption of moisture and separation of fibers. In (b), note the marked twisting on the long axes.

wound around the cone. This gives the cone-shaped or spiral strand of suture material, the diameter of the spiral decreasing from the base toward the apex. When the catgut is withdrawn and tension made on the material to draw it to a relative straight condition, thus flattening the coils, there is an increase in the amount of twist originally applied to the strand in its manufacture.

Number 1 chromic catgut, of several manufacturers, has been used in these experiments. The material was removed from the tubes, wound in the manner described above and placed in 95 per cent alcohol until used. It was prepared under strict aseptic conditions and buried in the wounds of animals.

In one series of experiments, material was taken from the tube of a 60-inch strand and divided into two equal parts. One-half of the material

was then wound with the increase twist procedure. Knotted loops were made from both pieces of the material and tied under five pounds' tension. These loops were inserted into the abdominal wall of guinea-pigs and specimens taken at various intervals (Fig. 3). Experimental loops of the twisted material were found to be turned upon their long axes while the standard material remained almost circular after several days' stay in the wound. The loops of twisted gut withstood digestion and retained their continuity, on an average, five days longer than the loops made from the conventional material.

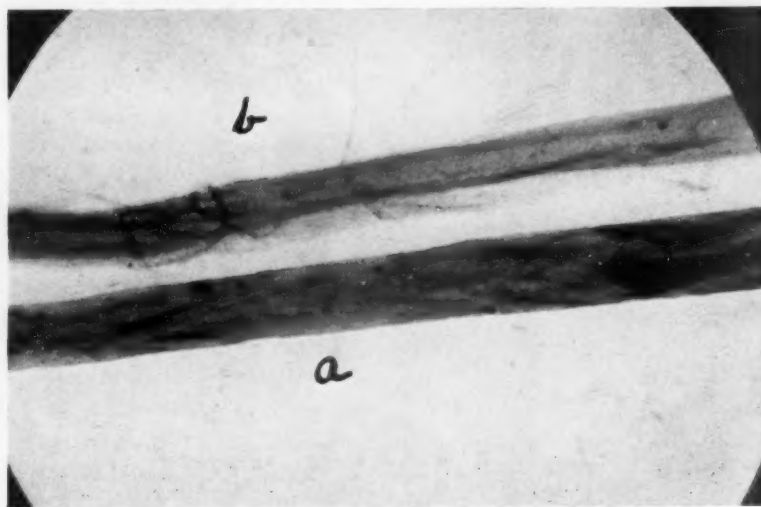


FIG. 4.—Photomicrograph following the 2 per cent trypsin-tension test. (Mounted in gum damar.)

Both segments were taken from the same 60-inch strand of material: (a) From material which had been spirally wound on a cone-shaped bobbin; (b) from the conventionally wound material.

These strands were threaded through capillary glass tubes, equal tension exerted on both, by means of mercury weights and then exposed to 2 per cent trypsin solution for a period of 48 hours.

Note the smaller frayed strand (b), in comparison to the experimental or spirally wound material (a).

In a series of experiments, straight strands of short, free pieces of conventionally wound material were buried in the abdominal wall of the dog along with an equal number of knotted loops of the same material. They were examined ten days later. In nearly every instance the loops were found, but practically all of the straight pieces of material had been absorbed. It is reasonable to assume that the knots preserved the twist in these loops. The loss of a knot in a ligature, with subsequent rapid absorption, may explain the absence of catgut so frequently encountered in cases which come to autopsy a few days after operation.

Trypsin Tests.—Sixty-inch strands of No. 1 chromic catgut were equally divided and one portion wound in accordance with the method described above. Small capillary glass tubes of equal length and diameter were

threaded over segments of both wound and unwound strands, which were then exposed to equal amounts of tension by means of mercury weights. These strands were then placed under the dissecting microscope, side by side, and 2 per cent trypsin solution introduced into the glass tubes by capillary attraction. Within a few minutes, considerable debris could be seen in the solution containing the conventional catgut material, while little precipitate was to be observed in the tube of the twisted strand. The diameter of the

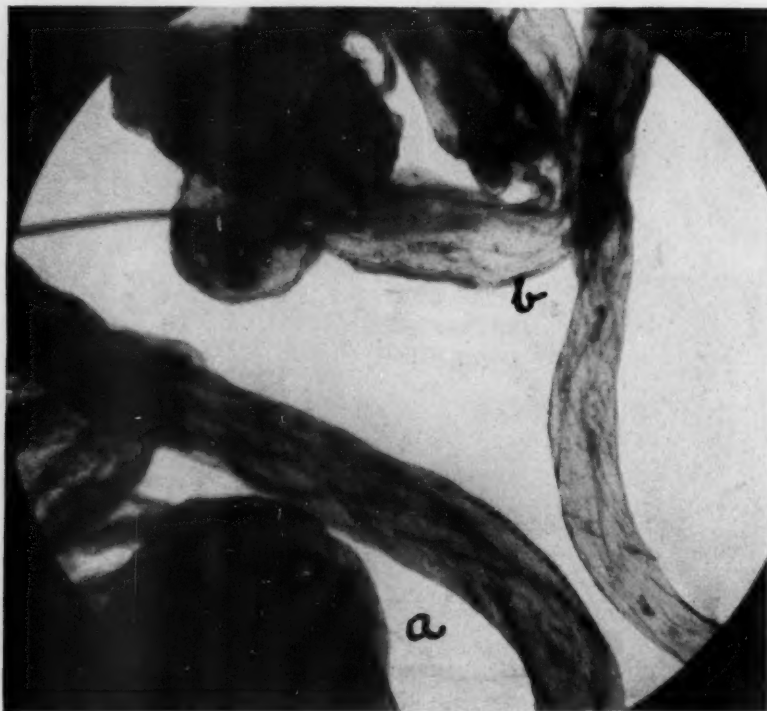


FIG. 5.—Photomicrograph of nonboilable No. 1 chromic catgut which had been placed in the peritoneal wound of a dog for a period of ten days. (Mounted in gum damar.)

One-half of the wound had been sutured with a continuous suture which had been taken from the conventionally wound material. The other half was sutured likewise with catgut which had been spirally wound on a cone-shaped bobbin. Both strands were obtained from the same 60-inch strand of material.

The knot (a) and its continuous portion is the spirally wound or experimental suture material, while the knot (b) and its continuous strand was taken from the conventionally wound catgut.

Note the difference in diameters and structure of the two sutures after ten days' stay in the wound.

conventional or control material was considerably less than that of the twisted material after two days' exposure to the solution. The surfaces of the standard or control strands were frayed and had a moth-eaten appearance. The digestion of the other material was slower and more uniform; the strands presented a smoother appearance (Fig. 4).

Number 1 chromic catgut was used in the peritoneum of rectus incisions of 196 dogs operated upon from 1927 to 1933, inclusive. Thirteen dogs with

infected wounds were discarded. The peritoneal wounds were sutured with catgut taken from the same strand in each individual experiment. One-half of the wound was sewed with a continuous suture of the conventionally wound material and the remaining half closed with the special twisted catgut. The wounds were reopened in ten days to two weeks after operation. Practically every animal showed remnants of varying degree of thickness of remaining catgut of both materials after ten days' stay in the wound.

In 16 experiments, there had been a separation of wound surfaces with adhesions of abdominal viscera in the portions sutured with the conventionally wound catgut. In the areas sutured with the special twisted material, four such instances were to be found. Adhesions of lesser degree were found in ten other cases of the entire group, but one was not able to definitely attribute this to any fault in suture technic. Microscopic sections of the knots and sections of the ligatures were also studied. Details are to be found in the captions to Figure 5.

Clinical Experiences.—During the past 16 years, the author has personally tied the more important knots in a selected series of abdominal cases which include 25 rectus or midline wounds, 75 McBurney incisions and 50 incisions for inguinal hernia. The patients were operated upon in six different hospitals and their progress observed from one to five years after operation. The knots used were square ones consisting of three loops or throws (Fig. 2). The first throw was tied in the right hand or clockwise direction with particular care to produce tension by pulling the hands in a plane parallel to the structure being ligated. The second throw of the knot was tied counter-clockwise (left hand throw) and the loop drawn only fairly tight. The third loop of the knot was then tied as in the first, *i.e.*, clockwise direction with tension estimated to be approximate to the amount used in the first throw. Thus the first and third throws are tied in the corresponding direction of the twisted material. In the first loop of the knot after crossing the ligature, the catgut was spun clockwise in the right hand and counter-clockwise in the left hand as it was being drawn taut. The rotation of the catgut between the thumb and index finger as mentioned above prevents to a certain extent the unwinding of the twist in the material when the first throw of the knot has been applied. The loss of twist at the point near the knot no doubt is of considerable importance in the process of disintegration. It has been the common experience of all to see the continuity of the material broken at this point.

In the 100 cases of rectus, midline and McBurney wounds there were no postoperative herniae. In the 50 hernial wounds, two recurrences were found: one, subsequent to a secondary infection, the other, a latent recurrence following a fall. Number 1 chromic catgut, of various manufacturers, was used in practically all of the 150 cases.

It is to be admitted that the writer has had the usual number of post-operative abdominal herniae secondary to drainage in peritoneal infection. However, since the publication⁶ of the work (1924) on drainage of abdominal

wounds, no herniae have developed in those cases where that described procedure has been used. During the past 16 years, the writer has had no cases of postoperative disruption of abdominal wounds in noninfected cases. This may be attributed to the careful application of catgut and to the particular attention to exact detail in tying knots.

SUMMARY

(1) The conventional method of spinning catgut suture material is the right hand or clockwise procedure.

(2) Review of the literature shows varied and divergent results in regard to hydrolysis or absorption of catgut.

(3) Very little information is to be found on the absorption of catgut in terms of the tensile strength.

(4) Only one article on thorough experimental work pertaining to catgut knots was to be found (Taylor,¹⁷ 1938).

(5) Experimental and clinical data are presented to show that the loss of the twist in the catgut suture material is an important factor to be considered in the reliability and the absorption of the material.

(6) The loss of twist in catgut suture material exposes more surfaces of the suture or ligature to the influence of the tissue juices.

(7) Square or reef knots may be tied with the first throw of the knot applied either in the right hand (clockwise) or left hand (counter-clockwise) direction.

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ANNOUNCEMENT OF A STUDY TO EVALUATE ORIGINAL SEROLOGIC TESTS FOR SYPHILIS

U. S. PUBLIC HEALTH SERVICE

WASHINGTON, D. C.

MORE than five years ago, the Committee on Evaluation of Serodiagnostic Tests for Syphilis, in coöperation with the United States Public Health Service, conducted a study to evaluate original serologic tests for syphilis, or modifications thereof, in the United States. The results of this study were published shortly after the investigation was completed.¹

Consideration is now being given by the Committee to the organization of a second evaluation study of original serologic tests for syphilis, or modifications thereof, within the next year. If the need for an investigation of this kind seems to justify the cost, invitations will be extended to the authors of such serologic tests who reside in the United States, or who may be able to participate by the designation of a serologist who will represent them in this country. The second evaluation study will be conducted utilizing methods comparable to those employed in the first study.²

Serologists who have an original serologic test for syphilis, or an original modification thereof, and who desire to participate in the second evaluation study, should submit their applications not later than October 1, 1940. The applications must be accompanied by a complete description of the technic of the author's serologic test or modification. All correspondence should be directed to the Surgeon General, United States Public Health Service, Washington, D. C.

*Thomas Parran, M.D.,
Surgeon General*

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227 South Sixth Street, Philadelphia, Pa.